Wounds

Definition :
It is forcible loss of continuity of soft tissues by mechanical trauma.

Classification :
[A] Open wounds : associated with loss of the continuity of the skin.
[B] Closed wounds : associated with intact skin.

[A] Open wounds : Are either incised, stab, lacerated or gunshot.
1. Abrasion : Partial denusion of superficial layers of skin due to friction of skin with a rough surface.
2. Incised wounds : due to sharp objects are liable for more bleeding & less liable for infection.
3. Stab or punctured wounds : is caused by pointed objects as nails and daggers.
4. Lacerated wounds :
- They are caused by blunt heavy objects.
- These wounds are **less liable for profuse bleeding** (as the blood vessels are crushed).
- **More liable for infection** whether nonspecific or specific as tetanus & gas gangrene.

5. Missile wounds :
- They have an inlet (for entry of the bullet) and may have an exit.
- The damage is due to the following factors :

(a) Direct damage by missile track.
(b) Shock waves preceding missile injury to the body.
(c) Temporary cavitational effect.
(d) If bone affection; bone fragments act as secondary missiles.

- The degree of injury by the missile depends on its size and velocity :

(a) Low velocity missile : e.g. bullet from a pistol produces injury due to its direct effect by laceration and crushing within the passage of the missile.
(b) High velocity missile : Tissue necrosis occurs several centimeters on either side of the track due to the cavitation effect. It is more lethal.
6. Bites : either human or animal bites. They are very liable to infection.

[B] Closed wounds :
1. Contusion = Ecchymosis : It is extravasation of blood from injured small blood vessels with no formation of a swelling.
2. Hematoma : Localized collection of blood in the loose tissue spaces.

Complications of wounds

General complications :

1. Shock : Neurogenic, hypovolemic or septic shock.

2. Crush syndrome :
Etiology :
- Prolonged ischemia with irreversible muscle necrosis.
- Toxic substances from damaged muscles leak out into circulation & are excreted in urine.
- Acid myohematin precipitates in the tubules producing anuria & irreversible renal failure.

Treatment :
(a) Prevention of renal failure : By alkalanization of urine, blood transfusion, IV fluids & mannitol.
(b) Care of the injured limb :
i. Should be immobilized & kept cool. ii. Care of the wounds.

Local complications :

1. Injury to important structures. 2. Infection.
3. Retained foreign bodies. 4. Complications of healing.

Management of open wounds

I- First aid treatment :

1. Control bleeding by compression.
2. Protect the wound from contamination.
3. Analgesics for pain.
4. Splintage of fracture if the wound is associated with it i.e. compound fracture.

II- Definitive treatment :

- **Do 3 anti :** (anti-shock, anti-biotics and anti-tetanic serum).

1. Clean cut (incised wounds) within the first 6 hours :

- No contamination and no risk of infection.
- **The edges of wound are approximated by suture.**
- **Tendons and nerves can be sutured.** This aims at healing by primary intention

2. Lacerated wound within the first 6 hours :

- **The edges of the wound** are excised and primary suture of the wound is done.
- **Tendons and nerve repair** is postponed 4 – 6 weeks.

3. Wounds seen within 24 hours and are potentially contaminated :

- **The dead muscles** and **dead tissues** are excised, **foreign bodies** are removed.
- **The wound is left opened** for dressing with no suture for 4-6 days.
- **When healthy granulation fills the wound delayed primary suture can be done.**

4. Infected wounds :

- **Debridement** is done in which only dead and devitalized tissues are removed.
- **No excision** of the edges of the wound is done, as this will break the body defense against infection.
- **Daily dressing** is done.
- When the wound gets cleaner it can be **closed by suture or by skin grafting.**

5. Missile injuries :

- **Incise the skin** generously but do not excise much skin from the wound margin.
- **Incise the deep fascia** widely and identify the neurovascular bundles.
- **Excise dead muscles and foreign bodies** but do not remove comminuted bone. Cut tendons and nerves are not sutured.
- **Leave the wound open** to allow free drainage.

6. Amputation :

- Indicated in severely lacerated wounds with comminution of bones and injury to the blood supply and nerves of the limb that cannot be repaired.

N.B.:

1. If there is any doubt about the advisability of suturing the wound, do not suture. Primary suture of a contaminated lacerated wound can lead to more damage than the original injury.

2. If there is an associated fracture and there is any possibility of infection, it is advisable to stabilize the fracture by some form of external fixation, because internal fixation is contraindicated in these circumstances.

Wound healing & management

Wound healing

Components of wound healing :

1. **Wound contraction :** helps to diminish the size of wound.
2. **Granulation tissue formation :** which is replaced later by **fibrous tissue.**
3. **Epithelialization.**

Stages of wound healing :

1. Hemostasis & inflammation phase :

- Injury of blood vessels leads to aggregation of platelets & activation of coagulation.
- This is followed by **chemotaxis** of leucocytes, macrophages & lymphocytes.
- Macrophages play an important role in phagocytosis & wound debridement.
- This phase **lasts for about 5 days,** but it may be prolonged if there is wound infection.

2. Proliferation phase :

- This phase is characterized by the proliferation of **fibroblasts** that secrete collagen fibers.
- **Endothelial cells with fibroblasts** form the granulation tissue.
- **Epithelial cells proliferation.**

3. Maturation & remodeling phase :

- **Deposition of the collagen fibers become thicker** and they get **arranged along the lines of stress** leading to increase in the tensile strength of the wound.
- The process of remodeling continues **for about one year.**

In addition to the above mechanisms, wound contraction helps to diminish the size of wound.

Types of wound healing :

1. Healing by primary intention : This occurs in clean wounds when they are immediately closed by sutures or clips. Healing occurs with minimal scarring leading to a nice scar.

2. Healing by secondary intention : This occurs when the wound edges are not approximated or when gaping occurs as a result of a hematoma or wound infection. Healing occurs by infilling with granulation tissue and so there is more fibrous tissue. The resulting scar is ugly.

3. Healing by tertiary intention : potentially contaminated wounds are left open for about 5 days. At the end of this period if there are no signs of infection; **delayed primary sutures** can be performed.

Factors affecting wound healing

I- General factors :

1. Age : Wound healing is slow in elderly persons due to a reduced rate of protein turnover.

2. Nutritional state :

(a) Protein deficiency leads to diminished synthesis of collagen.
(b) Vitamin C deficiency is responsible for lack of maturation of collagen.
(c) Vitamin A deficiency leads to deficient epithelilization.
(d) Calcium, zinc, copper & manganese also affect wound healing.

3. Debilitating diseases : Uremia, jaundice, cirrhosis, diabetes & malignancy delay wound healing.

4. Drugs : Steroids and cancer chemotherapy impair wound healing.

II- Local factors :

1. Vascularity : A good blood supply (e.g. in the face & scalp) leads to nice healing while a poor blood supply (wounds below the knee) causes delayed healing.

2. Immobilization : Movement delays healing.

3. Local irradiation : Inhibits wound contraction & granulation tissue formation.

4. Tension : Any increased tension in the wound will lead to ischemia & impaired healing.

5. Infection : Fibroblasts compete with bacteria for oxygen & nutrition. Moreover, bacteria secrete collagenolytic enzymes, which destroy collagen fibers.

6. Foreign bodies & necrotic tissue : impair wound healing.

7. Adhesion of wound to a bony surface : Prevents wound contraction e.g. chronic venous ulcers.

8. Impaired venous drainage : as in postphlebitic limbs impairs wound healing.

Complications of healing :

1. Wound failure (wound dehiscence) : General or local factors which affect wound healing can lead to wound failure. Failure of an abdominal wound is called burst abdomen.

2. Stretching of the scar.

Items	3. Hypertrophic scar	4. Keloid
Definition	**Delayed maturation** of collagen fibers in a wound.	**Failure of maturation** of collagen fibers in a wound.
Induration	Limited to the scar.	Extends beyond the scar.
Course	Stationary after 6 months.	Progressive even after 6 months.
Sites	Common in shoulder & presternal area.	Ear lobules, shoulder, presternal area.

Incidence of Keloid :
Black persons are more prone to keloid formation and there is a familial predisposition.

Treatment of hypertrophic scars and keloids :
(a) Continuous pressure by silicone gel sheets.
(b) Intralesional corticosteroids.
(c) Surgical excision : Recurrence rate after simple excision may reach 80%. To minimize recurrence intramarginal excision of the scar is recommended together with intraoperative injection of steroids.

5. Contracture : resulting in deformities.

6. Wound infection.

Accident & Emergency Surgery

Introduction :

- Trauma is now a leading cause of mortality and morbidity, especially in urban areas.
- Unfortunately, most of the victims of trauma are young persons.
- With proper treatment many injured patients can be saved.

Mechanism of injury :

1. Penetrating injuries :

- Low velocity injuries caused by knife & other sharp objects.
- High velocity injuries caused by firearms.

2. Blunt injuries : e.g. road traffic accidents, fall from a height or direct blows.

Causes of trauma mortality :

1. Immediate deaths : occur within few minutes due to major trauma or injuries to the heart, rupture of a major vessel or a major airway.
2. Early deaths : occur within hours after accident & can be prevented by rapid, proper management & it include intracranial hemorrhage, massive intra-abdominal or intra-thoracic injuries or major fractures.
3. Late deaths : occur some weeks after the injury usually due to sepsis or multiple organ failure.

Organized trauma care :

N.B.:

- **Check that the airway is patent :** Support the mandible forwards; suck any secretions in the mouth. **If necessary insert an oropharyngeal airway.**
- **During transfer of the patient,** care should be taken to avoid flexion of the spine that may lead to dislocation in unstable spine injuries. **If a cervical spine injury is suspected, a rigid cervical collar is applied.**

- Victims of major trauma are best treated by a well-organized and trained **trauma team.**
- Accident and emergency departments should have an equipped **resuscitation area** to receive major trauma victims.
- In mass casualty accidents, the concept of **triage** is important. Triage means sorting of patients, i.e., their ranking according to both their clinical need and the available resources to provide treatment.

- The American College of Surgeons developed the **Advanced Trauma Life Support (ATLS)** accepted protocol for the management of major trauma victims. ATLS protocol has three elements :

1. Primary survey / resuscitation.
2. Secondary survey.
3. Definitive care of individual injuries.

[1] Primary survey/ resuscitation :

Objective : to identify & treat any immediately life threatening conditions.
Steps : ABCDE
A – **A**irway (& cervical spine control).
B – **B**reathing.
C – **C**irculation with hemorrhage control.
D – **D**isability (neurological assessment).
E – **E**xposure & **E**nvironment.

[A] Airway :

- **Clear airway :**

1. Vomitus, blood or foreign material should be removed.
2. This is followed by chin lift or jaw thrust.

- **Airway & cervical spine control :**

1. Suck any secretions or blood in the mouth or remove by finger.
2. Chin lift.
3. Insert an oropharyngeal airway.
4. If the patient is deeply comatosed insert a cuffed endotracheal tube.

Tracheal intubation is indicated with:

a) Apnea
b) Risk of aspiration
c) Impending or actual airway compromise (inhalation injuries, maxillofacial trauma)
d) Closed head injuries (allow hyperventilation to decrease intracranial pressure)

N.B 1: ***orotracheal intubation*** allows the use of a large tube.
N.B 2: ***nasotracheal intubation*** is safer if the cervical spine appears fractured.

5. It is rarely necessary to do a **tracheostomy** as a first aid measure, but if needed it can be performed later as an elective procedure after the airway is established. If urgently needed, a **cricothyroidotomy** is a similar and faster procedure.
6. Cervical spine immobilization if needed is done by using a backboard & a rigid collar.

[B] Breathing :

- **Assessment :**

1. **Inspection** for chest movement, respiratory rate, cyanosis, open wounds & expansion.
2. **Palpation** for subcutaneous emphysema & flail segments.
3. **Percussion** for hyperresonance or dullness.
4. **Auscultation** for air entry & adventitious sounds.

- **Life threatening conditions in chest injuries management :** (see chest injuries).

[C] Circulation : This entails :

1. Control of hemorrhage (discuss).
2. Anti-shock measures.
3. CPR for cardiac arrest.
4. ECG monitoring.

[D] Disability : (Brief Neurological Examination)

AVPU Evaluation : according to best response, it is classified as follows :

- **A**lert & interactive.
- **V**ocal stimuli elicit a response
- **P**ainful stimuli are needed to produce a response
- **U**nresponsive.

[E] Exposure & Environment :

1. Remove all clothes using sharp large scissors.
2. Keep the victim & place warm to avoid hypothermia.
3. Insert urethral catheter & nasogastric tube.
4. Radiological examination.

5. Proper history taking AMPLE :

- **A**llergies, **M**edications, **P**ast medical history, **L**ast meal time & **E**vents of injury.

[2] Secondary survey :

- **Objectives :**

1. Full patient examination.
2. Complete medical history.
3. Integration of all available data.
4. Formulation of a management plan.

- **It includes examination of :**

1. Head & neck.
2. Face & spine.
3. Chest & abdomen.
4. Perineum (including rectal & vaginal examinations).
5. Nervous system.
6. Limbs : for fractures & soft tissue injuries.

[3] Definitive treatment of individual injuries : according to its site (see before).

Fluid, electrolytes & acid-base balance

Physiological considerations

Body water :

- Total body water varies from 45 – 75% of body weight.
- 2/3 of the water is intracellular while the other 1/3 is extracellular.
- Extracellular fluid is subdivided into the interstitial compartment & intravascular compartment.
- Water distributes freely & its source is either exogenous or endogenous.
- Water loss is usually through lungs, skin, feces & urine.

Electrolyte :

Sodium :

- Main extracellular cation that plays the main role in maintaining blood volume.
- Adrenal corticoids, mainly aldosterone, control reabsorption of sodium in renal tubules.

Potassium :

- The major intracellular cation.

Calcium :

- Serum calcium (8.5 – 10.5 mg/dl) is found in ionized & non-ionized (protein bound) forms.
- Alkalosis decreases the ionized form & may lead to tetany.
- It is controlled by vitamin D, PTH, Calcitonin, kidney & small bowel state.

Acid – Base regulation : (7.4 ± 0.04)

- Renal regulation by HCO_3 reabsorption & H^+ excretion.
- Respiratory regulation by rate of CO_2 elimination.

Diagnosis of imbalances

History : e.g., vomiting, diarrhea, or excessive sweating.

Clinical signs :

- Vital signs, pulse and blood pressure.
- Urine output & Tissue turgor.
- Edema & crepitations.
- Central venous pressure (CVP), and pulmonary artery wedge pressure (PAWP)

Laboratory values :

- Hematocrit & hemoglobin.
- Serum sodium & potassium.
- Arterial blood gases (ABGs) to obtain Blood pH, PO2 and PCO2& HCO3.

Water imbalance

Water depletion (Pure dehydration)	Water excess (water intoxication)
Causes	**Causes : Often iatrogenic e.g.:**
1. Lack of water intake. 2. Diabetes insipidus. 3. Increased output e.g. in fever & osmotic diuretic.	1. Over-infusion of 5% glucose solution to postoperative patients. 2. Colorectal washouts with plain water. 3. TURP syndrome (transurethral resection of prostate).
Clinical Picture	
1. Intense thirst and weakness. 2. Decreased tissue turgor. 3. Oliguria.	1. Increased urine volume. 2. An increase in body weight. Pitting edema usually does not develop. 3. Decreased serum sodium concentration and falling hematocrit value. 4. Rarely, swelling of brain cells leads to drowsiness, weakness & convulsions and coma (Water intoxication).
Management	
Na–free water according to the estimated deficit. If water depletion is severe, at least 1/2 of the estimated deficit should be replaced in the initial 12 hours of treatment. 5% glucose is given IV.	1. Restriction of water intake. 2. Forced diuresis with Mannitol. 3. In severe cases IV administration of small amounts of 5% sodium chloride solution.

Sodium imbalance

Sodium depletion (Hyponatremia)	Sodium excess (Hypernatremia)
Causes	
1. Abnormal gastrointestinal tract losses (Suction, vomiting and diarrhea). 2. Loss of ECF, either externally (burns, marked sweating) or internally as a third space (peritonitis, ascites or ileus). 3. Excessive urine sodium loss e.g. (diuretics). 4. Blood loss. 5. Restricted dietary intake. 6. Adrenocortical insufficiency.	1. Giving excessive amount of 0.9% saline solution intravenously during the early postoperative period. 2. Hyperaldosteronism : 1ry (Conn's syndrome) or 2ry to liver cirrhosis. 3. Cushing's syndrome.
Clinical Picture	
1. Eyes are sunken. In infants the anterior fontanel is depressed. 2. The tongue is coated and dry. 3. Peripheral veins are collapsed. 4. Hypovolemia, with low CVP, results in tachycardia, orthostatic hypotension and shock. 5. There is hemoconcentration with normal or slightly reduced serum sodium.	1. Slight puffiness of face is the only early sign. 2. Edema, the only reliable clinical sign. 3. Weight gain. 4. Hypertension. 5. Serum sodium concentration is usually normal.
Treatment	
1. Restoration of ECF volume by appropriate amounts of Na–containing fluids such as normal saline (NaCl 0.9%) or Ringer's lactate. 2. Blood losses should be replaced.	1. Sodium restriction. 2. Diuretics.

Potassium imbalance

Potassium depletion (Hypokalemia)	Potassium excess (Hyperkalemia)
Causes	
1. Vomiting as occurs in gastric outlet obstruction, e.g. pyloric obstruction. 2. External GIT fistulae 3. Diarrhea especially when severe. 4. Certain types of diuretics as frusemide. 5. Alkalosis & Hyperaldosteronism.	1. Renal failure. 2. Acidosis. 3. Diabetic patients.
Consequences	
1. Raises membrane excitation potentials, making nerves & muscles less excitable. 2. Risk of supraventricular arrhythmias. 3. Increases the susceptibility of hepatic coma in patient with liver disease.	1. Stimulation of aldosterone secretion (K^+ level 5mmol/L). 2. Decreases membrane excitation potentials, making cells more excitable.
Clinical Picture	
1. Most patients are asymptomatic. 2. Malaise and weakness. The speech is slow. 3. Paralytic ileus and distension may be seen. 4. Muscular paresis appears only with extreme depletion. 5. ECG reveals prolonged QT interval, depression of the ST segment, and a lowering or inversion of the T wave.	If the serum potassium exceeds 7mmol/L, intracardiac conduction is slowed and arrhythmia, bradycardia and hypotension may be followed by cardiac arrest. The ECG is a sensitive investigation for hyperkalemia. It shows a wide QRS complex and peaked T waves.
Treatment	
• The required quantity of potassium is added to the infusion and distributed all over the day. • Potassium should never be injected as a bolus. • **Safe rules for giving potassium are :** 1. Urine output at least 40 ml/hour. 2. Not more than 40 mmol added to 1 liter. 3. No faster than 40 mmol/hour.	1. IV calcium gluconate as calcium antagonizes potassium. 2. IV sodium bicarbonate. 3. Dextrose and insulin infusion. 4. If the previous measures fail, they should be followed by giving exchange resins, 5. If all the previous measures fail to lower the serum potassium, dialysis should be started.

Calcium imbalance

Hypocalcemia :

- **It may be :** transient or latent.
- **Due to :** hypoparathyroidism, acute pancreatitis & acute alkalosis.
- **Clinical Manifestations :** hyperactive deep tendon reflexes, muscle & abdominal cramps, carpopedal spam & rarely convulsions. Positive Chvostek's sign can be elicited.
- **ECG :** shows prolonged QT interval.
- **Treatment :**

1. In acute cases : correction of underlying cause & IV injection of calcium gluconate or calcium chloride.
2. In chronic cases : vitamin D, oral calcium supplements & aluminum hydroxide gels are given.

Postoperative fluid and electrolyte therapy

In prescribing fluid regimens for postoperative patients, three points are considered :
1. Basal requirements.
2. Pre-existing dehydration, electrolytes loss and acid-base disturbances.
3. Continuing abnormal losses.

The daily requirements of water and electrolytes in an adult are :
Water : 35mL/kg **Sodium :** 1 mmol/kg **Potassium :** 1 mmol/kg

The usual daily postoperative fluids for uncomplicated surgery in an adult :
1. Three liters of fluids. Add 200ml per day for each 1°C rise in temperature.
   - 500 ml saline (0.9% NaCl) provides the daily requirements of Na & Cl.
   - The remaining volume requirement (2.5 L) is given as 5% dextrose (glucose).
2. Potassium supplements are given after 48 hours

Preoperative evaluation of hemostasis

History :
1. Family history of bleeding & history of bleeding tendency.
2. Age at onset of bleeding.
3. History of chronic liver & renal failure, massive blood transfusion and drug intake.
4. Characters of the bleeding :
- Defects of 1ry hemostasis (platelet/vessel abnormalities). Bleeding is superficial.
- Defects of 2ry hemostasis (coagulation/fibrinolysis). Bleeding is deep.

Examination :
1. Signs of liver disease.
2. Skin and mucous membranes are examined for bleeding, petichae, or bruising.
3. Cavernous hemangioma may trap platelets leading to thrombocytopenia.
4. Musculoskeletal system e.g. hemoarthrosis (coagulopathy).

Tests of Hemostasis :
[A] Tests of primary hemostasis :
1. Platelet count & bleeding time.
2. Bone marrow aspiration and biopsy.
3. Tests of platelet function (adhesion, release, aggregation).

[B] Tests of secondary hemostasis : PT, PTT & TT.

Hemorrhage

Classification of hemorrhage

Hemorrhage may be classified according to :
[1] Site :
1. External : Bleeding is visible as it occurs through the skin as in wounds or from a body orifice as in epistaxis or hematemesis.
2. Internal : Examples are hemoperitoneum and hemothorax.
3. Interstitial : Bleeding occurs into the tissues forming a hematoma. e.g. fracture hematoma.

[2] Type of disrupted vessel :

1. Arterial : The blood is bright red in color and comes in pulsatile jets. The bleeding is more from the proximal than the distal end.
2. Venous : The blood is dark red in color and comes as a steady flow. It is more from the distal than the proximal end.
3. Capillary : Bleeding occurs as diffuse ooze of bright red blood.

[3] Timing in relation to the onset of trauma :

1. Primary hemorrhage : occurs at the time of trauma.
2. Reactionary hemorrhage : occurs some hours after trauma (within 24 hours) due to slipped ligature or dislodged clot.
3. Secondary hemorrhage : occurs one to two weeks after trauma due to infection eroding a vessel wall.

[4] Etiology : Hemorrhage may be :

1. Traumatic.
2. Pathological :
- Atherosclerotic (ruptured aortic aneurysm).
- Inflammatory (bleeding peptic ulcer).
- Neoplastic (hematuria in renal cancer).

3. Bleeding diathesis : spontaneous hemorrhage.

[5] Hemorrhage can be classified into 4 classes :

Parameter	Class I	Class II	Class III	Class IV
Blood loss	Up to 15% (750ml)	15-30% (750-1500ml)	30-40% (1500-2000ml)	> 40% (2000ml)
Mental status	Normal to anxious	Anxious to restless	Aggressive to drowsy	Drowsy to unconscious
Skin	Normal	Pale & cold	Paler & colder	Pale & very cold
Capillary refill	Normal	>2 seconds	>2 seconds	>2 seconds undetectable
Pulse/min.	<100	100-120	120-140	>140
Systolic BP	N	N (Supine)	Low	Low
Diastolic BP	N	High	Low	Low
Pulse pressure	N	Low	Low	Low
RR	14-20	20-30	30-35	>35
Urine output	>30 ml/hr	20-30ml/hr	10-20ml/hr	0-10ml/hr

Physiological response, C/P, management : See hypovolemic shock.

Estimating blood loss : This is obtained from :
1. Clinical data.
2. Types of injury e.g. fracture of pelvis (2000 – 3000 ml).
3. Blood loss at operation is the sum of the amount in the suction reservoir and the amount mopped up by the swabs.

Investigations : A blood sample is obtained for :
1. Complete blood picture, including hematocrit.
2. Coagulation profile.
3. Cross matching.

Excessive operative & postoperative bleeding

Causes :

1. Inadequate surgical hemostasis(commonest cause).
2. Hemorrhagic diathesis not detected preoperatively.
3. Acquired intraoperative coagulopathy e.g. DIC & massive blood transfusion.

Management :

1. Replace amount of blood loss.
2. PT, PTT & platelet count.
3. Fresh Frozen Plasma (FFP) 3-4 units initially & Platelet transfusion if needed.
4. Proper surgical hemostasis.

Surgical hemostasis

During surgery the bleeding is controlled by one of the following methods :

1. Ligation.
2. Under-running suture.
3. Electrocautary (diathermy) : to stop bleeding from small blood vessels, either Monopolar or Bipolar.
4. Clips, Laser.
5. Repair of injured large vessels (see arterial).

N.B: Primary hemostasis is achieved by:VC ,platelet plug and tamponade by surrounding tissue tension.
Secondary hemostasis is achieved by:coagulation.

Blood transfusion

Blood components :

1. Packed red cells : The transfusion of packed red cells is very useful in anemic patients, in the elderly and in cardiac patients as it improves the oxygenation ability without overloading the circulation.
2. Fresh plasma : It is rich in platelets and coagulation factors.
3. Fresh frozen plasma : Plasma removed from fresh blood is rapidly frozen and stored at - 40°C. It is a good source of all the coagulation factors.
4. Platelet concentrates : Should be freshly prepared as half life of platelets is very short.
5. Cryoprecipitate : This is prepared from fresh frozen plasma and is very rich in factor VIII and fibrinogen. It is stored at -40°C.

Indications for transfusion of blood & its products :

	Indication	Precautions	Storage
Whole blood	Class III & IV hemorrhage.	ABO & Rh incompatibility.	21 days.
Red cell concentrates	Severe anemia.	ABO & Rh.	21 days.
Fresh frozen plasma	1. Bleeding due to non-specified coagulation factor deficiency. 2. Coumarin overdose.	ABO	One year at -40°C.
Platelets concentrates	Primary or secondary thrombocytopenia.	ABO	24-72 hours.
Cryoprecipitate of factor VIII & fibrinogen.	Bleeding with fibrinogen depletion.		One year at -40°C.
Factor VIII	Hemophilia A		2 years
Factor IX	1. Hemophilia B. 2. Coumarin overdose.		
Albumin 5% or 20%	Hypoalbuminemia		2 years

N.B.: It is no longer recommended to transfuse fresh blood to correct coagulopathies. The specific deficient component should be used.

Complications of blood transfusion :

Though generally safe and simple, the procedure of blood transfusion is not free of complications. The majority of these are simple, yet some are immediately fatal and others produce chronic serious illness as hepatitis and AIDS. Attention to strict rules of donation and administration of blood greatly reduces the incidence of these complications.

I- In the donor :

1. **Neurogenic shock.**
2. **Anemia** if repeated amounts are taken.
3. **Local thrombophlebitis** in the veins.

II- In the recipient :

1- Immunological complications of blood transfusion:

- Incompatible red cells lead to acute hemolytic reaction.
- Incompatible white cells lead to pyogenic reaction.
- Incompatible platelets lead to purpura.
- Reaction to a protein in the plasma leads to allergic reaction.

a) Hemolytic reactions :

Due to: presence of antibodies in the recipient's blood against antigens in the donor's cells.

Clinically:

- After the transfusion of less than 50 ml : fever, chills, constricting pain in the chest, dyspnea and pain in the flanks.
- In anesthetized patients : there will be sudden tachycardia, hypotension & bleeding tendency.
- A major hemolytic reaction : will lead to hemoglobinuria, jaundice & acute renal failure.

Management:

- Stop the transfusion immediately.
- Repeat typing.
- Correct shock by infusion of crystalloid solution (Lactated Ringer) & IV corticosteroids.
- An osmotic diuretic as mannitol may be needed. Keep urine alkaline to protect against ARF
- If ARF develops, it must be treated.

b) Pyrogenic reactions: (The most common complication)

C/P : Chills, fever, headache, nausea and vomiting.

Due to : presence of recipient antibodies against the donor's WBC's or bacterial contamination.

c) Allergic reactions:

C/P : Range from mild itching & urticaria to severe reaction with laryngeal edema & collapse.

Due to : The recipient's response to allergens in the donor's blood.

Treatment : Is by antihistaminics and corticosteroids. If the reaction is severe, blood transfusion should be stopped.

d) Post transfusion purpura.

2. Congestive cardiac failure :

Occurs in : elderly persons especially if a large volume of blood is administered too rapidly.

C/P : See medical notes.

Prevention : It is recommended to transfuse packed red cells rather than whole blood to correct anemia in elderly persons.

3. Transmission of infection :

- **Viral hepatitis (B or C) :** This is now the most feared complication. Whole blood or blood products can transmit the virus. It is now obligatory to test donor for hepatitis viruses.
- **AIDS infection.**
- **Septicemia :** Bacteria can survive, but they cannot multiply significantly in refrigerated blood. However, if the blood is allowed to warm, bacteria can grow and Gram-negative endotoxins can cause septicemic shock.

4. Hyperkalemia :

- With prolonged storage of blood, there is progressive loss of potassium from erythrocytes into plasma.
- Transfusion of several units of aged blood may produce cardiac arrhythmias or even arrest due to hyperkalemia.

5. Citrate intoxication :

- Excess citrate will bind to the recipient's calcium leading to hypocalcemia that augments the effects of hyperkalemia on the myocardium.
- **Prevention:** If more than 2 units of blood are administered, it is important to administer 10 ml of 10% calcium gluconate for each two units of blood.

6. Air embolism.

7. Transfusion-related acute lung injury (TRALI)

Due to incompatibility between donor's antibodies and recipient granulocytes.
Clinical picture: as ARDS.

8. Complications of massive blood transfusion:

Definition : Transfusion of 2500 ml of blood at one time or 5000 ml or more over 24 hours.
1. Hypothermia: A special warming unit should be used to warm blood before transfusion.
2. Hyperkalemia.
3. Hypocalcemia.
4. Coagulation failure: As stored blood is poor in platelets, factor VIII & factor V. In these situations it is recommended to transfuse one unit of fresh frozen plasma and platelets for every unit of stored blood.
5. Diminished O2 carrying capacity of RBC's.

The physiological changes which occur during blood storage :

Items	0 day	7th day	14th day	21st day
% Of red cells viability	95%	90%	85%	75%
% Of platelets viability	95%	0%	0%	0%
% Of coagulation factor V & XIII	95%	30%	30%	30%
Potassium content (mmol/L)	3.5	10	25	30

How to minimize the need for homologous blood transfusion ?
1. Autologous blood transfusion : the patient who is going to have a major elective operation, can donate some units of his own blood over several days. The blood is kept in the refrigerator to be given back to him during surgery.
2. Preservation of the blood lost during surgery and its reinfusion to the patient. This needs a special apparatus **(cell saver).**

Shock

Definition :

Shock is a pathophysiologic condition that leads to inadequate tissue perfusion through the microcirculation with impaired cellular metabolism.

Classification :

1. Hypovolemic shock
2. Cardiogenic shock
3. Neurogenic shock
4. Anaphylactic shock
5. Septic shock
6. Endocrinal shock

I- Hypovolemic Shock

It is due to diminished blood volume, which may occur secondary to loss of :
1. Blood : As in internal or external hemorrhage.
2. Plasma : As in bums and peritonitis.
3. Fluids : As in severe vomiting, diarrhea & intestinal obstruction.

Physiological response to hemorrhage : (The classical example of hypovolemic shock)

- **The physiological response to hemorrhage is :**

[1] Stopping the bleeding : by immediate vasoconstriction and retraction of the intima with subsequent clotting. These mechanisms are more effective when the vessel is completely transected than when there is a side tear, and in traumatic than in pathological cases.

[2] Maintaining effective circulatory volume & perfusion of critical tissues (brain & heart), at the expense of less critical tissues (skin, skeletal muscle & splanchnic area).

- **This is achieved by :**

[A] Neural factors : Stimulation of the sympathetic system, with the following effects :
1. Constriction of veins displaces blood from the capacitance side of circulation into the heart.
2. Constriction of arterioles raises the peripheral resistance. It involves mainly the arterioles of the skin, skeletal muscle, and splanchnic area.
3. Increased rate and strength of cardiac contraction.
4. Transcapillary refill : Constriction of arterioles causes a fall in capillary hydrostatic pressure and promotes movement of fluid from the interstitium into the capillaries.

[B] Endocrine response : Is mediated through the following mechanisms :
1. Catecholamine : They increase the heart rate and myocardial contraction and cause constriction of the arterioles of the skin, kidney and viscera.
2. ACTH, Cortisol, growth hormone & glucagon are increased : Leading to hyperglycemia which increases extra-cellular fluid (ECF) osmolarity & withdraws water from the intracellular fluid (1CF). This increases effective blood volume.
3. The renin-angiotensin aldosterone system : Angiotensin II is a powerful vasoconstrictor and stimulates sodium and water retention by a direct action on the kidney as well as indirectly through release of aldosterone.
4. Vasopressin (ADH).

These mechanisms allow survival without therapy for losses up to 15% of the blood volume.

[3] Microcirculatory changes :
1. Under the effect of catecholamines the precapillary sphincters constrict.
2. Untreated hypovolemia thus leads to hypoxia. Under ischemic conditions, the body reacts by opening more capillaries. **The results are :**
   - Further slowing of capillary circulation
   - Spontaneous coagulation of blood in these capillaries. If extensive, it is called disseminated intravascular coagulation (DIC).
3. A sluggish circulation & DIC aggravate tissue hypoxia and affect the function of capillary endothelium.

[4] Cellular Derangement :
1. Lack of oxygen forces the cells to rely on anaerobic glycolysis which produces lactic acid.
2. With persistent hypoxia, cellular functions start to deteriorate.
3. The end result is rupture of lysosomal and plasma membranes and cell death.

[5] Acid-base imbalance : Shock is accompanied by metabolic acidosis, which is caused by :
1. Accumulation of lactic acid. 2. Renal failure.

[6] Effect on individual organs : (see later)

Clinical picture :

Symptoms :

1. **Weakness and fainting** especially when standing.

N.B: hypotension in supine position in a fit patient means a loss of at least 1500 ml of blood.

2. The patient feels **cold and thirsty.**

Signs :

1. The mental status : may vary from anxious to drowsy but the patient usually remains alert.

2. Pulse and blood pressure : With mild blood loss (less than 500 ml), the pulse & blood pressure may remain normal. With more blood loss, tachycardia develops but blood pressure remains stable. With more progressive blood loss, progressive hypotension develops.

3. Pulse pressure (PP) : decreases leading to a thready pulse.

4. Respiratory rate : Tachypnea & air hunger due to chemoreceptor stimulation by hypoxemia & acidosis.

5. Temperature : Hypothermia occurs.

6. Skin : becomes pale, cold (vasoconstriction) & clammy with slow capillary refill & collapsed veins.

7. Oliguria.

- **If the patient is rapidly treated by adequate volume replacement,** his vital signs will rapidly return to normal.

- **If not, the following will occur :**

1. The heart : Myocardial contractility is impaired by direct myocardial depressants as cachectin, tumor necrosis factor (TNF).

2. Intestine : translocation of depressing substances (bacteria and endotoxins) from the ischemic gut into the circulation that may be a factor in the development of multiple organ system failure.

3. Stomach : true stress ulcers.

4. The liver : ischemic Hepatic dysfunction is a frequent component of MOSF.

5. Renal affection : Prolonged hypotension ends in acute tubular necrosis which is a part of the multiple organ system failure.

6. Pulmonary response : ARDS occur as pan of MOSF.

Irreversible shock

- Complete vascular collapse with hypotension unresponsive to volume or drug intervention leading to lethal central nervous system and cardiac dysfunction.

- **It is related to :**

1. The duration and volume of hemorrhage.
2. The age.
3. Pre-existing cardiovascular fitness of the patient.
4. The presence of massive trauma.

- **Before the conclusion that irreversible shock has occurred, other causes of failure to respond to therapy should be resolved :**

1. Continuing unsuspected blood loss into the chest or abdomen.
2. Inadequate volume replacement.
3. Occult thoracic injuries including cardiac tamponade.
4. Acute myocardial insufficiency.

Monitoring the severely shocked patient :

- **The aim is to check the adequacy of replacement :**

1. Clinical parameters : Pulse, blood pressure, state of filling of veins, capillary perfusion and urinary output every hour.

2. Central venous pressure (CVP) : To measure the CVP, a cannula is placed in the right atrium via the median-cubital vein, the subclavian vein or the internal jugular vein. The normal pressure is 5-10 cm of water. Assuming that cardiac function is normal a high pressure indicates overtransfusion and the possibility of pulmonary edema, while a low pressure indicates hypovolemia.

3. Pulmonary artery wedge pressure (PAWP) : By the use of a **Swan-Ganz catheter.**

4. ECG.

5. Temperature : A simple non-invasive method of assessing cardiac output and peripheral perfusion is to measure the difference between the peripheral and core rectal temperature.

6. Blood gases :

- **PO_2** is normally between 80-100 mmHg.
- **PCO_2** is normally between 35-45 mmHg.

7. Repeated hematocrite & hemoglobin.

Treatment of hypovolemic shock :

[1] Stop the hemorrhage (if the cause of shock was hemorrhage, the classic example of hypovolemic shock) :

(A) First-aid treatment :

1. By packing, pressure, and position.
2. A skin wound is covered by a dressing (any clean material), and pressure is applied manually, by a sphygmomanometer cuff or by a bandage.
3. Elevation of the limb above the heart level stops venous & decreases arterial bleeding.

- **Tourniquets are contraindicated :** due to complications unless the limb is going to be amputated.

(B) Operation includes :

1. Primary hemorrhage : It is treated by controlling the bleeding point either by ligature or diathermy coagulation.

2. Reactionary hemorrhage : Open the wound & deal with the bleeding vessel as above.

3. Secondary hemorrhage :

- The wound is packed with antibiotics and sterile dressing.
- Antibiotics are given systemically.
- If the bleeding is not controlled in this way → re-open the wound and drain the infection. The vessel is then exposed & the wound is ligated.

[2] Restore the blood volume :

Volume replacement depends on the class of the hemorrhage :

Class II hemorrhage (15-30% Blood Loss) :

- The replacement solution is lactated Ringer's.
- The amount is 3 times the estimated deficit (~ 3L).
- Administration : Two liters are given as a bolus and the response is monitored. If there is definite improvement, the remaining liter is given more slowly, (a hematocrit <30 requires blood transfusion).

Class III and IV hemorrhage (30-40% & Blood Loss of > 40%) :

- The management is as for class II but these patients need blood transfusion.
- The initial volume of transfused blood is that of the estimated deficit (1500 - 2000 ml).
- Clean blood in the thorax or abdomen can be aspirated, anticoagulated and then transfused back into the patient (auto-transfusion) if a cell-saver is available.
- In the absence of whole blood : many substances have been proposed as human plasma, albumin solution, dextran and artificial blood substitutes.

[3] Positioning :

- Elevate both legs while maintaining the trunk and the remainder of the patient in the supine position.

[4] Pulmonary support :

- Oxygen is administered through a facemask, nasal catheter or an endotracheal tube.

[5] Analgesia :

- Morphia 3-5 mg (poorly absorption from subcutaneous sites), Morphine is contraindicated in head injury and in cases of respiratory and liver insufficiency.

[6] Inotropics : They are the second line of treatment.

- Dopamine & dobutamine are the most widely used; both improve myocardial contractility, while dopamine ↑ renal blood flow.

[7] Monitoring.

II- Septic Shock

This is the most serious type of shock and the most difficult to treat, having an overall mortality exceeding 30% and is exceeding 80% if with MOSF.

Etiology :

- **The incidence of Gram – ve sepsis is rising due to :**

1. Development of resistant and virulent organisms.
2. Concentration of infected patients in critical care units.
3. More extensive operations in elderly and poor-risk patients.
4. Salvage of severely injured patients.
5. Patients who are immunosuppressed by organ transplantation, radiotherapy and chemotherapy.

- **Predisposing factors :** Old age, diabetes mellitus, corticosteroids, chemotherapy & malignancy.
- **Causative organisms :** 1. Gram – ve bacilli (commonest). 2. Staphylococci. 3. Candida.
- **Source of Gram –ve sepsis :**

1. Peritonitis caused by perforated viscus, gangrenous bowel or leaking anastomosis.
2. Cholangitis or genitourinary infections.
3. Infected central venous catheter.

Pathophysiology :

[A] Mediators cascade :

Under the influence of endotoxins, macrophages release **cytokines** that cause the following major problems :

1. Platelets and leucocytes adherence to the vascular endothelium which leads to :

- Impairment of microvascular perfusion.
- Local release of cytokines and free oxygen radicals that damage the vascular endothelium.

2. Damage of the barrier function of the intestinal mucosa allowing intestinal pathogens into the circulation.

3. Excessive production of nitric oxide by the vascular endothelium which is a potent smooth muscle relaxant leading to the decreased peripheral resistance.

[B] Microcirculation :

1. Under the effect of cytokines vasodilatation of the arteries occurs and arterio-venous shunts are opened. The results are :

- Reduced peripheral resistance.
- Capillaries are bypassed & Oxygen delivery to the tissues is impaired.

2. Disseminated intravascular coagulation (DIC) is the result of sluggish capillary circulation.

[C] Cellular derangement : (see hypovolemic shock)

It is to be noted that oxygen uptake & utilization by cells is also directly suppressed by the toxins.

[D] Acid-Base imbalance. (see hypovolemic shock)

[E] Individual systems and organs. (see hypovolemic shock).

Clinical picture :

Hyperdynamic (warm) septic shock	Hypodynamic (cold) septic shock
Diagnosis is difficult and a high index of suspicion is required to detect cases at this early stage.	If the previous stage is not treated efficiently, the patient will develop a picture similar to that of hypovolemic shock with reduced cardiac output.
Clinical picture	
• Fever above 38°C and chills. • Patient is flushed with warm dry extremities. • Restlessness and confusion.	• Cold clammy skin.
• Mild reduction in blood pressure. • The cardiac output is elevated.	• Systolic blood pressure < 90 mmHg.
• Tachycardia and tachypnea.	• Tachycardia and tachypnea.
• Oliguria.	• Oliguria.
	• Multiple organ failure starts at this stage **(MOSF).**
Treatment	
• Prompt and aggressive treatment of the patient at this stage can lead to survival.	• Efficient and early treatment of the patient at this stage, can convert him to the hyperdynamic stage. • The mortality rate of a septicemic patient with multiple organs failure exceeds 80%.

Diagnosis : Helped by :

1. Polymorphnuclear leucocytosis.
2. Finding high lactate level in blood.
3. Looking for a source of sepsis.
4. Repeated blood culture at the peak of fever or culture from the septic focus.

Monitoring : See hypovolemic shock.

Treatment :

- **It is better to treat these patients in an intensive care unit.**

I- Support of different systems :

1. Cardiovascular support :

- Fluid replacement :

1. Prompt correction of fluid deficit is essential.
2. Ringer's Lactate is usually used.
3. Huge quantities of fluids are often needed
4. The amount often exceeds 10L within a few hours.
5. Packed R.B.C.'s transfusion may be indicated in cases with low hematocrite.

- Medications :

Inotropic drugs as dopamine & **vasopressor drugs** as norepinephrine can be used in patients with persistent life threatening hypotension inspite of active measures of treatment.

2. Respiratory support : Oxygen administration is essential for all types of shock. Usually 100% oxygen is administered as a start, and is later adjusted according to the response. If the arterial oxygen is mildly reduced oxygen by mask will be sufficient. Reduction of its level below 60 mmHg calls for endotracheal intubation and mechanical ventilation.

3. Renal support : Adequate volume replacement & dopamine administration improve renal blood flow.

II- Fighting infection :

1. Immediate recognition and early eradication of the source of sepsis.

2. Antibiotics : The choice of antibiotics will depend on the possible suspected organisms. The most commonly used combination is cephalosporin, aminoglycosides & metronidazole.

- **N.B.: Steroids are not indicated in the treatment of septic shock.**

III- Cardiogenic Shock

Here there is inadequate blood flow to vital organs due to inadequate cardiac output, despite a normal blood volume.

Causes :

1. Acute myocardial infarction (commonest cause).
2. Massive pulmonary embolism.
3. Cardiac tamponade.
4. Severe arrhythmia.
5. Improper treatment of hypovolemic shock may lead to cardiogenic shock.

- **Cardiogenic shock is characterized by congested neck veins and a high CVP.**

Treatment :

- See treatment of infarction.
- Drugs to improve myocardial contractility (inotropics).
- Vasodilators to reduce after load increase cardiac output and decrease myocardial work.

IV- Neurogenic Shock

There is paralysis of the vasomotor fibers leading to peripheral pooling of blood and inadequate venous return. **It may be due to :**

1. Vasovagal attack :

- It may follow hearing bad news, seeing an unpleasant event. Or sever painful stimuli.
- There will be extensive vasodilatation in the splanchnic area and excessive vagal stimulation of the heart that causes bradycardia.

2. High transection of the spinal cord or a complication of high spinal anesthesia.

> **N.B.: In neurogenic shock there is hypotension, normal pulse rate or bradycardia and warm dry skin.**

Treatment :

- The patient should lie flat with elevation of the legs.
- I.V. crystalloid solution as Ringer's lactate.
- Vasopressors may be prescribed.

V- Anaphylactic Shock

The patient develops bronchospasm, laryngeal edema and respiratory distress. Massive vaso-dilatation occurs and there is hypotension.

Treatment :

- Intravenous hydrocortisone.
- Antihistaminics.

VI- Endocrinal Shock

This may occur in patients with Addison's disease or those receiving continuous cortisone therapy if they are subjected to any stressful situation

Surgical infections

Diagnosis of surgical infections :

1. Clinical examination.
2. Laboratory studies (e.g. leucocytosis).
3. Imaging studies.

Principles of treatment :

1. Incision and drainage.
2. Excision.
3. Antibiotics.
4. General supportive measures.

Complications of surgical infections

1. Spread of infections occur by several mechanisms :

(a) Direct :

- Necrotizing infections.
- Abscesses.
- Phlegmons : these contain little pus but much edema.

(b) Lymphatic spread : producing lymphangitis with the characteristic red streaks in the skin that travel proximally.

(c) Blood stream : produces pyemic abscesses, Bacteremia & septicemia.

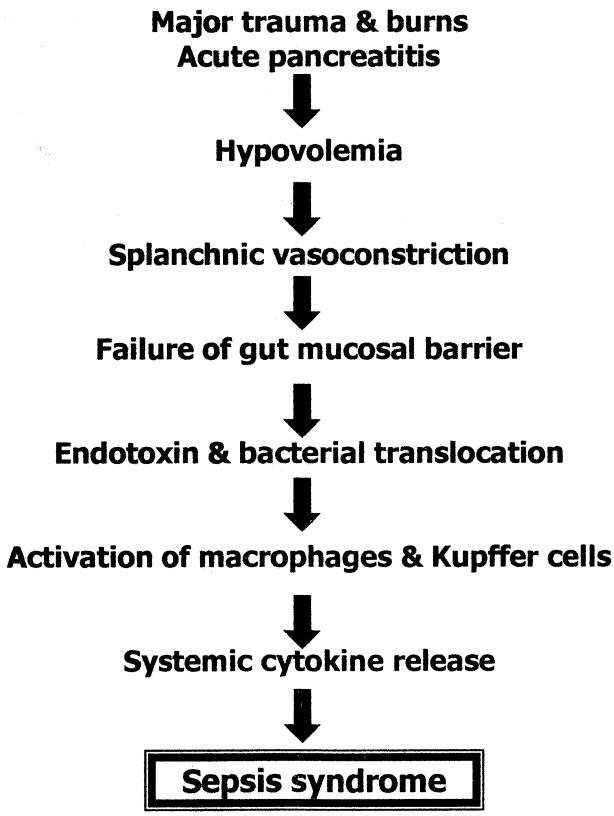
2. Fistulae & sinus tracts : e.g. a neglected anal abscess ends in an anal fistula.

3. Necrosis or gangrene of the affected part.

4. Suppressed wound healing.

5. Immunosuppression & superinfection.

6. Systemic inflammatory response syndrome and multiple organ failure **MOSF.**



Non-specific acute infections
Surgical site infections (SSIs)

This is a serious problem that may complicate operative wounds, which may even cause mortality in severe cases.

Contaminating microbes may be derived from :

1. The patient himself (endogenous).
2. From his environment (surgical team, instruments, dressings...etc.)

Predisposing factors :

General factors :

1. Poor general condition.
2. Systemic diseases that impair host defense as diabetes mellitus or uremia.
3. Drugs that cause immunosuppression as corticosteroids or chemotherapy.

Local factors :

1. Poor blood supply.
2. Poor surgical techniques e.g. rough handling of tissues.
3. Presence of foreign bodies as prosthetic implants.
4. Nature of the operation, e.g. operations for peritonitis.
5. Defect in the sterilization technique in the operating theatre.

Types of surgical wounds :

1. Clean	2. Clean contaminated	3. Contaminated
• Herniorrhaphy. • Thyroidectomy.	• Urological or Oropharyngeal procedures. • Surgery on prepared colon.	• Surgery on unprepared colon. • Operation on grossly infected area of body e.g. surgery for peritonitis.
No gross contamination from endogenous or exogenous sources.	Wounds involve regions of the body that may contain low numbers of resident organisms.	An unprepared region of the body with large numbers of endogenous organism is entered.
The risk of infection is 1-2%.	The risk of infection is 2-5%.	The risk of infection is 5-30%.

4. Dirty wounds e.g.: traumatic wounds more than 4 hours, and perforated viscus accompanied by high degree of contamination. Risk of infection is up to 40%.

Clinical picture :

Usually appears between the 5th & 10th days postoperatively :

1. Postoperative fever.
2. The wound is painful, swollen, tender and red.
3. Fluctuant areas or crepitus can occasionally be felt.

Differential diagnosis :

1. Other causes of postoperative fever e.g. chest infections, DVT etc.
2. Other causes of wound swelling e.g. hematoma.

Prophylaxis :

1. Any predisposing factor should be controlled : e.g. diabetes, malnutrition & anemia.
2. Prophylactic antibiotics are indicated in :
(a) Clean contaminated or contaminated surgery.
(b) In wounds where foreign material is implanted.
3. Before any elective colorectal surgery, preparation of the bowel is recommended.
4. Proper surgical technique : e.g. gentle handling of tissues, adequate hemostasis.

Treatment :

1. The wound should be opened and stitches removed to allow pus drainage.
2. Antibiotics guided by culture and sensitivity tests.
3. Possible sources of hospital infection should be traced and corrected.

Cellulitis

Definition : This is an invasive non-suppurative infection of the loose connective tissue.

Organism : Gram-positive bacteria mostly streptococci or occasionally staphylococci introduced into the superficial skin structures.

The portal of entry : May be trivial, e.g. scratch or prick.

Clinical picture :

1. The affected area is red or reddish brown, indurated, hot and painful.
2. It spreads rapidly and the advancing edge is ill defined.
3. There is no suppuration, except occasionally at the portal of entry.

Treatment :

1. Antibiotic (penicillin group).
2. Rest and elevation.
3. Hot packs.
4. Careful follow-up is needed in order not to miss a hidden abscess.

Erysipelas

Definition :

This is a rapidly spreading non-suppurative inflammation of the lymphatics of the skin.

Organism :

Specific strain of hemolytic streptococci.

Route of entry :

Through minute scratch or abrasion.

Clinical picture :

- **Symptoms of toxemia are present.**
- **Locally the picture is similar to cellulitis but there are the following differences :**

1. The color of the skin is rose-pink.
2. The edge is well defined, slightly raised and often shows minute vesicles just behind the spreading margin.
3. There may be islets of inflammation beyond the spreading margin separated from the main area by apparently normal skin.

Treatment :

1. The patient needs to be isolated because the disease is very contagious.
2. Similar to cellulitis.

Boil (Furuncle)

- This is a staphylococcal infection of a hair follicle or a sebaceous gland.
- More common in diabetics and whenever there is lack of personal hygiene.
- Necrosis of the central part occurs and is discharged together with a small bead of pus.

Treatment :

1. Antibiotics effective against Staph. organisms, incision may be needed.
2. Icthiol ointment and warm foments.
3. Painting the surrounding skin with an antiseptic to prevent infection of the neighbouring glands or hair follicles.
4. Always suspect diabetes mellitus in patients who develop recurrent boils.

Carbuncle

Definition :
Localized infective gangrene of the skin and subcutaneous tissues.

Pathology :
1. Route of infection : through hair follicles as a furuncle spreads to subcutaneous tissues and other hair follicles.
2. Predisposing factors : diabetes is the most important factor.
3. Sites : hairy areas with thick skin e.g. face, back of neck (nape), back of fingers & the back.
4. Naked eye appearance : Infection starts in the root of a hair follicle. This may lead to thrombosis of the blood vessels, leading to ischemia of the overlying skin resulting into infective gangrene of skin and subcutaneous tissues. Sloughing of the skin leads to multiple discharging openings on the surface.
N.B.: Infective gangrene may develop in the kidney leading to carbuncle of the kidney or cortical abscess.

Clinical picture :
- It is more in males especially diabetics.

Symptoms :
- Patient complains of a furuncle that resists treatment & extends to other hair follicles.
- Severe pain aching in nature (not throbbing).
- Multiple discharging openings.

Signs :
- Skin is dusky in color.
- Mild swelling with multiple sinuses discharging sloughs, usually no frank pus.
- Marked diffuse tenderness.
- Indurated swelling.

Complications :
1. **Local spread of infection** leads to cellulitis and lymphangitis.
2. **Pyemia and septicemia.**
3. **Carbuncles of the dangerous area of the face** can lead to cavernous sinus thrombosis.
4. **Carbuncles of the back of the neck** may rarely lead to epidural abscess or meningitis.

Treatment :
1. **Antibiotics** effective against resistant Staph. organisms.
2. **Culture and sensitivity** of the discharge.
3. **Proper control of diabetes mellitus** if present.
4. **Glycerin magnesia & local foments help** in the separation of the sloughs
5. **Excision of sloughs.**

Hydradenitis Suppurativa

- Mixed Staph. and streptococcal infection of the apocrine sweat glands, in the perineum or the axilla, produces multiple abscesses and pus-discharging sinuses. Infection is difficult to eradicate and the case usually progresses to chronicity with considerable fibrous tissue reaction.
- In the perineum, hydradenitis suppurativa is often misdiagnosed as multiple anal fistulae. Careful examination reveals the absence of internal anal openings.
- **Treatment** by drainage of abscesses followed by careful hygiene, painting with disinfectants and antifungal applications may be enough. Otherwise, excision of the apocrine sweat-bearing skin followed by skin grafting is essential.

Necrotizing fasciitis

Etiology :

- Invasive infection, caused by a mixed microbial flora including microaerophilic streptococci, staphylococci, Gram-negative bacteria and anaerobes, especially peptostreptococci, and bacteroids.
- The organisms gain access through a wound usually in immunocompromised patients.

Pathology :

- The infectious process spreads along fascial planes & results in infectious thrombosis of vessels.
- Superficial skin necrosis. Hemorrhagic bullae appear as the first sign of skin death.
- Fascial and subcutaneous fat necrosis involves an area wider than the skin.

Clinical features :

- The patient is alert and fully conscious with manifestations of toxemia.
- The skin shows hemorrhagic bullae and necrosis surrounded by edema and inflammation.
- Crepitus is occasionally present and the skin may be anesthetic.

Investigations :

- Gram stained smears and cultures
- At surgery the finding of edematous, dull gray fascia and subcutaneous tissue with visible thrombi in penetrating vessels, confirms the diagnosis.

Prevention :

- Adequate debridement of wounds, blood loss replacement and antibiotics for contaminated wounds are essential to prevent postoperative necrotizing fasciitis.

Treatment :

- **Surgical treatment :** Debridement, under anesthesia is essential.
- **Antibiotics :** Penicillin intravenously together with gentamycin or Amikacin.
- **Blood transfusion, nutritional support and control of diabetes if present.**

Prognosis :

- In many cases the diagnosis is missed.
- In elderly patients, the disease is likely to have a fatal outcome.

Acute Abscess

- It is a localized suppurative inflammation.
- The commonest causative organisms are staphylococci

Pathogenesis :

The organisms reach the tissues by :

1. Direct access through wounds.
2. Local extension from an adjacent focus
3. Lymphatic spread.
4. Blood spread.

Pathology :

An abscess consists of three zones :

1. A central zone of coagulative necrosis.
2. An intermediate zone of granulation tissue.
3. A peripheral zone of acute inflammation.

Fate :

1. Resolution if treated.
2. Pointing and rupture (commonest sequel).
3. Spread of infection.
4. Chronicity.

Clinical Picture :

1. Painful tender mass, skin is red & edematous.
2. The draining lymph nodes are usually enlarged and tender.
3. A systemic reaction in the form of fever, malaise, headache, tachycardia and anorexia.

When pus forms :

1. The pain becomes throbbing.
2. The fever becomes hectic.
3. The covering skin shows pitting edema.
4. The inflammatory reaction becomes localized.
5. Fluctuation can usually be elicited in a subcutaneous abscess.
6. There is shooting leucocytosis with shift to the left

Treatment :

1. Before suppuration : antibiotic, rest, hot application and general supportive measures.
2. After suppuration : Once pus forms, the only treatment should be free drainage.

Bacteremia & Septicemia

Bacteremia :

- Presence of bacteria that are not multiplying in the blood.
- It usually follows dental work and instrumentation of the urinary tract.
- Hazardous in patients with damaged heart valves or with prosthetic valves. Antibiotic prophylaxis is essential in such cases.

Septicemia :

- Presence of multiplying organisms in the blood stream plus leucocytosis.
- It usually denotes significant infection in which bacteria, bacterial toxins or inflammatory mediators escape the control of the immune system, enter the blood stream and produce a systemic response including chills, fever and sometimes, pulmonary failure or shock.

N.B.:

Toxemia : Presence of toxins in the circulation. It may be the only symptom of the patient or it may form part of local condition e.g. tetanus, gas gangrene, diphtheria.

Pyemia : The presence of septic emboli in the circulation and the formation of multiple pyemic abscesses. It is either systemic or portal pyemia.

Specific acute infections

Tetanus

Definition :

Tetanus is a specific anaerobic infection that is mediated by the neurotoxin of Clostridium tetani and leads to nervous irritability and tetanic muscular contractions.

Etiology :

Organism :

- Clostridium tetani is a gram-positive anaerobic bacillus with a terminal spore giving the characteristic drum - stick appearance.
- The organism is naturally present in the intestine of horses and the spores are present in manured soil and street dirt.
- The spores are resistant to antiseptics, heat, dryness and can resist boiling for 5 minutes.

Mode of infection :

1. Wounds : wounds contaminated with soil.

Wounds predisposed to tetanus :

- Wounds contaminated by the excreta of horses.
- The presence of foreign bodies or associated pyogenic infection.
- Wounds accompanied by low 02 tension locally e.g.:

i. Deep seated wounds.
ii. Lacerated wounds.
iii. Local decrease of the blood supply e.g. tight bandage and plaster of Paris.

- Decrease of the blood supply to the area by a systemic cause e.g.:

i. Hypotension or shock. ii. Anemia.

2. Umbilical stump :

- In old days catgut, prepared from the intestine of sheep and contaminated with tetanus spores, was responsible for some outbreaks of **tetanus neonatorum.**
- By contaminated dressings or powders.

Predisposing factors : The anaerobic organisms flourish more in wounds with low oxygen tension, e.g. tight bandages or shocked patients. The presence of a foreign body or associated pyogenic infection also predisposes to tetanus infection. Still, tetanus may follow a small abrasion.

Pathology :

- **The neurotoxin** is an exotoxin produced locally and reaches the central nervous system along the blood stream, the motor nerves or both.
- Once the toxin reaches the nervous system, it is at once **fixed by the motor cells** and can't be detected in the blood or CSF.
- **The tetanus antitoxin** can only neutralize the toxin before it gets fixed to the nervous tissue.
- **The toxin increases the excitability** of the motor cells of the medulla and spinal cord so the slightest stimuli produce violent spasm.
- **Death results from** exhaustion, hyperpyrexia, heart failure, asphyxia or pneumonia.

Clinical picture :

The incubation period :

- In the non-immunized the period is short and varies from 24 hours to 15 days.
- In immunized patients the period is longer than 11 days and may be several weeks or months.

Manifestations of tetanus are divided into :

1. Toxemia :

- Increased temp., patient is irritable & complains of headache, rigors and G.I.T. disturbance.
- Sometimes, patient gets myocarditis, nephritis, or liver failure secondary to toxemia.

2. Tonic stage :

- The first symptoms are usually pain and tingling in the area of injury.
- Limited movements of the jaw **(lock jaw, trismus).**
- Spasm of the facial muscles **(risus sardonicus).**
- These are followed by stiffness of the neck, difficulty in swallowing.

3. Clonic stage :

- Reflex attacks of violent muscular contractions.

The spasms are initiated by any form of stimulation such as bright light :

- Relaxation is incomplete during the intervals between clonic contractions.
- During these spasms the body may be arched backwards **(opisthotonos).**
- Spasms of the intercostal muscles and diaphragm occur & leads to longer periods of apnea.
- The temperature is normal or slightly elevated.
- Sweating is profuse.
- Marked tachycardia is a grave sign.

Special types of tetanus :

1. Chronic tetanus : The incubation period is more than 2 weeks, the symptoms are much less severe and there are no reflex spasms. The prognosis is favorable.

2. Local tetanus : This occurs in immunized persons where immunity counteracts the general toxemia. The spasms are restricted to the muscles around the wound.

3. Cephalic tetanus : This rare type may follow wounds in the head and neck. The toxin is absorbed by the facial nerve which becomes edematous and compressed within the bony canal so that paresis of facial muscles occurs

4. Splanchnic tetanus : The muscles of deglutition and respiration are affected leading to dysphagia and fatal dyspnea.

5. Acute fulminating tetanus toxemia : It occurs in the non-immunized patients. It has short incubation period and marked toxemia. The patient may die before the appearance of convulsions, or convulsions develop early and rapidly.

6. Surgical tetanus : Occurs after surgical operation either due to the catgut used in the suture material or due to reactivation of dormant tetanus spores in an old wound by the recent operation.

7. Cryptogenic tetanus : This mild form may occur without an overt wound.

Complications :

1. Tear in the muscles.
2. Avulsion fracture of bones.
3. Toxic myocarditis.
4. Toxic nephritis.
5. Liver failure.

Laboratory findings : Polymorphnuclear leucocytosis may be present.

Differential diagnosis :

1. Trismus : due to local causes such as tempromandibular arthritis.

2. Meningitis : The neck muscles are affected first.

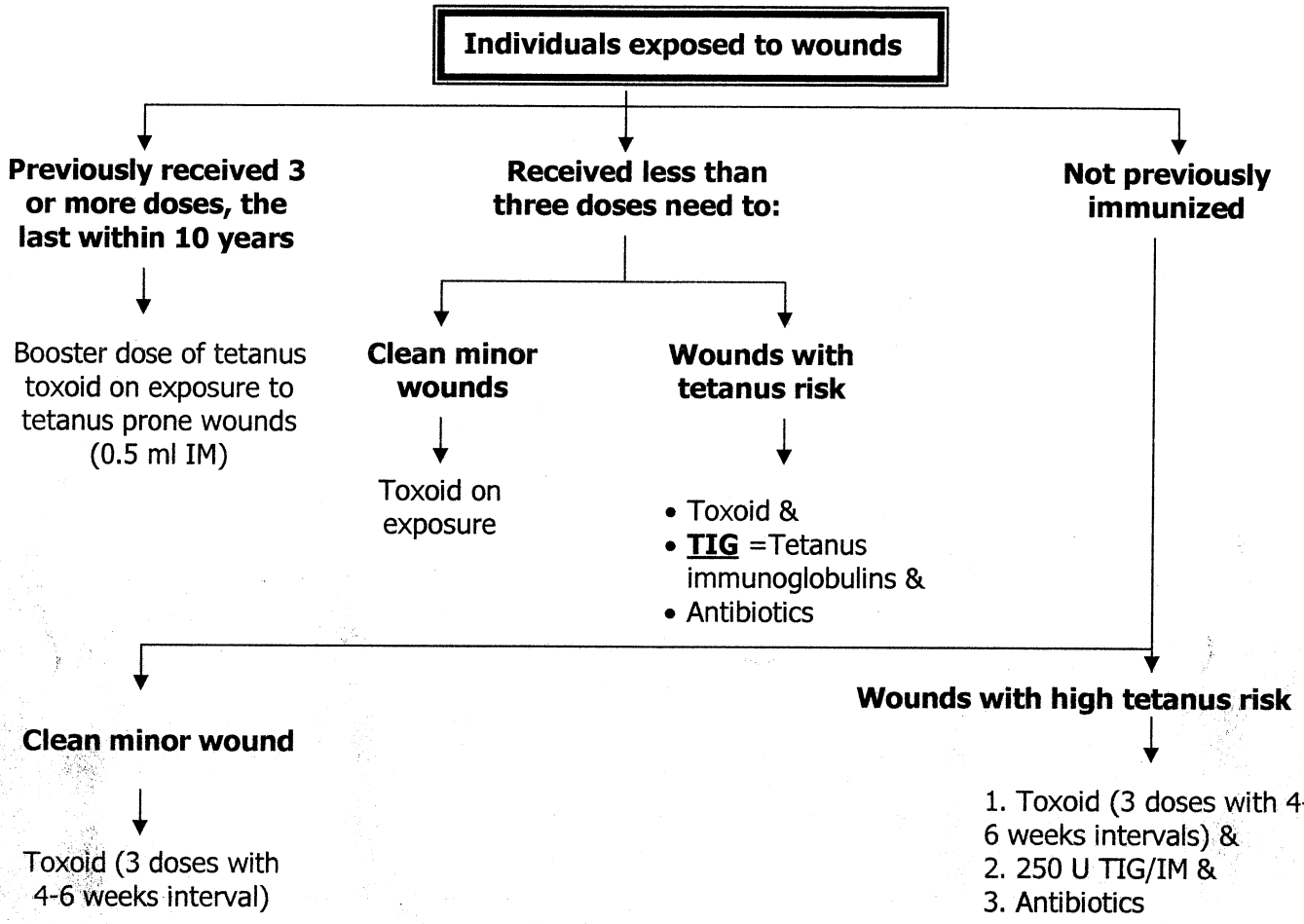
3. Strychnine poisoning : The spasms are entirely clonic with complete relaxation during the intervals.

4. Tetany : The hands and feet are mainly affected.

5. Rabies : There is history of a dog-bite: The spasms occur on seeing and drinking water. The muscles of deglutition and respiration are mainly affected.

Prevention :

Every child should be actively immunized with tetanus toxoid, beginning with routine childhood immunization and continuing with booster injections every 7-10 years.


Individuals exposed to wounds
Previously received 3 or more doses, the last within 10 years
Booster dose of tetanus toxoid on exposure to tetanus prone wounds (0.5 ml IM)
Received less than three doses need to:
Clean minor wounds
Toxoid on exposure
Wounds with tetanus risk
• Toxoid &
• TIG =Tetanus immunoglobulins &
• Antibiotics
Not previously immunized
Clean minor wound
Toxoid (3 doses with 4-6 weeks interval)
Wounds with high tetanus risk
1. Toxoid (3 doses with 4-6 weeks intervals) &
2. 250 U TIG/IM &
3. Antibiotics

N.B.:

1. TIG is given in a different syringe & at a different site & consider the use of antibiotics.
2. Other tetanus antitoxin (equine antitoxin) should be used only if TIG is not available & only after testing for hypersensitivity to the product.

Treatment : Intensive treatment should be started soon :

[A] Neutralize toxin with TIG (3000-6000 units IM) :

- Given preferably in the proximal portion of the wounded extremity or in an area near the wound.
- Repeated doses may be required.

[B] Excise and debride the wound under anesthesia :

- After neutralization of the toxin. The wound must be left open and may be treated with hydrogen peroxide.

[C] The patient :

1. Should be protected from sudden stimuli, unnecessary movements and excitement.
2. Nursing : The patient is isolated in a dark quiet room & nutrition is maintained by a naso gastric tube.
3. Barbiturates are used cautiously as they often cause cardiorespiratory failure.
4. Curarization with mechanical ventilation is a better alternative Adrenergic blocking agents may be needed in cases showing intense sympathetic stimulation.
5. Respiratory problems may require tracheotomy. The patient should be intubated once respiratory problems appear.
6. Aqueous penicillin G : 10-40 million units a day.

Prognosis :
The death rate is 30-60% in established cases.

Causes of death :
1. **Toxemia.**
2. **Respiratory obstruction** by aspiration of vomitus or persistent contraction of respiratory muscles.
3. **Starvation.**
4. **Exhaustion** from persistent muscle contraction.

• **One attack of tetanus does not give a life-long immunity. Patients who recover from an attack need to have an active immunization schedule.**

Gas Gangrene (clostridial myositis)

Etiology :
• Gas gangrene is an acute spreading gangrene, associated with gas formation and profound toxemia, due to infection of extensive wounds by anaerobic spore-bearing bacilli of the clostridium group.
• **Toxins responsible :** The alpha toxin is particularly important but other toxins including collagenase, Hyaluronidase, leukocidin, protease, lipase and hemolysin also contribute.

Factors predisposing to gas gangrene :
• It is closely associated with grossly contaminated war injuries and is now a major concern with terrorist attacks on civilian population.
1. Lacerated wounds involving bulky muscles as in the gluteal area and thigh.
2. Presence of foreign bodies or devitalized tissues.
3. Ischemia of the muscles e.g. due to injury of the main vessels, tight bandages or cast or sutures under tension.
4. Infection by aerobic bacteria, which make the medium suitable for the anaerobic clostridia.
5. Gas gangrene may follow above knee amputation especially in elderly persons who may suffer from fecal incontinence leading to infection of the stump.

Source of the organism :
• Some of the clostridia are normal inhabitant of the intestine of man and animals.
• Manured land e.g. farms and field battle.

Bacteriology and pathology :
I- Local Effect : Organisms causing gas gangrene fall into two groups:
[A] Saccharolytic organisms : include Cl. welchii, Cl. septicum & Cl. edematiens.
These organisms cause :
• Necrosis of muscle from thrombosis of blood vessels and hemolysis of blood.
• Ferment the glycogen of the dead muscles with liberation of carbon dioxide and hydrogen.
• The liberated blood pigments stain the dead muscle fibers by a brick red color.
[B] Proteolytic organisms : include Cl. sporogenes, Cl. Histolyticum.
These organisms ferment the proteins of dead muscles with liberation of :
• Ammonia that neutralizes the acid products of saccharolytic organisms.
• Hydrogen sulphide gas which combines with iron leading to the formation of iron sulphide that produces greenish black discoloration.

II- Systemic Effects :
• Blood hemolysis leads to pallor and a tinge of jaundice.
• Degenerative changes occur in the liver, kidneys and suprarenal glands.

Clinical picture :

The incubation period : Varies from few hours to few days.

Generally :

- The patient is pale. anxious and apprehensive.
- The temperature may be raised and there is marked tachycardia.
- The hands are cold and clammy.
- An icteric tinge may be present and there is oliguria.
- In severe cases the patient is shocked.

Locally :

- Pain and numbness in the affected area.
- The wound is swollen and there may be crepitus with gas bubbles.
- A sanguinous discharge of a characteristic odor may exude from the wound.
- The affected muscles show brick red then greenish and finally black discoloration. They do not contract on pinching and do not bleed if cut.
- The skin overlying the wound may show greenish or black discoloration.

Differential diagnosis :

[A] Other clostridial infections :

1. Simple contamination :

- Many open wounds are superficially infected or contaminated with clostridia without developing significant infections.
- These surrounding tissues & simple debridement of the dead surface tissue are enough treatment.
- The infection can turn into an invasive type.

2. Gas abscess (Welch's abscess) :

- This is a localized non-invasive infection with no muscle involvement.
- Incision and drainage together with penicillin administration control the infection.

3. Anaerobic (Clostridial) cellulitis :

- It is localized to the subcutaneous tissue and is always superficial to the deep fascia.
- Edema & discoloration of skin with gas production & crepitus & no associated myositis.

4. Localized clostridial myositis :

- Although there is muscle involvement, the infection is not invasive.

5. Edematous gangrene :

- This type is produced by Clostridium oedematiens and is characterized by marked edema of the muscles with no gas production & is highly fatal.

[B] Non clostridial infections :

1. Gas producing infections :

- Are usually caused by a mixture of Gram-negative bacilli and Gram-positive cocci.
- These infections are not as virulent as gas gangrene & respond well to incision & drainage.

2. Surgical emphysema : Presence of gas under the skin.

Investigations :

The proper diagnosis of clostridial gas gangrene depends mainly on the clinical appearance of the wound and the presence of large Gram-positive rods on stained smears of exudate or tissue.

Prevention :

- All clostridial infections are preventable :

1. Adequate debridement of wounds : All dead muscles (do not bleed on cutting and do not contract on pinching) should be debrided and the wound properly cleaned, and left open.
2. Antibiotics : Especially penicillin.
3. Adequate circulatory support in severe injuries is required to avoid tissue hypoxia.

N.B.: Anti gas gangrene serum is no more used in modern surgical practice.

Treatment :

[A] Wound management : This is the most important step. Under general anesthesia :
1. The wound is opened and all dead tissues and muscles are excised.
2. Tight fascial compartments are decompressed.
3. The deep fascia and skin are left open.
4. Daily examination and debridement under anesthesia may be necessary.
5. Amputation :

- When there is diffuse myositis with complete loss of blood supply.
- When adequate debridement leaves a useless limb.

6. Diverting colostomy :

- When the source of the clostridial infection is an associated injury of the colon or rectum.
- In extensive perineal infections.

[B] Hyperbaric oxygenation : Hyperbaric oxygen inhibits bacterial invasion and the production of alpha toxin. Hyperbaric oxygen at 3 atm is given for 1-2 hours and is repeated every 6-12 hours. Three to five exposures are usually necessary.

[C] Fresh blood transfusions : Should be given early.

[D] Antibiotics : Penicillin 20 - 40 million units/day is given intravenously. Clindamycin or metronidazole can be used.

Prognosis :

1. Mortality Rate is about 20%.
2. The rate of salvage of functioning limbs is not favorable.

Actinomycosis

Etiology :

The causative organism :

- Actinomycetes, which are Gram-positive, filamentous organism.
- They are strict anaerobes and part of the normal flora of the human oropharynx & tonsils.

Mode of infection :

- In most cases the endogenous organism gain access through abrasions in the mucous membrane, but in some cases the lungs are infected by inhalation and rarely the skin is invaded by direct inoculation.

Pathology :

- The disease is characterized by inflammatory nodular masses, which may liquify to form abscesses and sinuses.
- The most characteristic feature is the presence of small yellowish granules known as **sulphur granules** in the tissues and in the pus.
- The granules consist of colonies of the organism, which appear as radiating Gram-positive filaments with club shaped Gram-negative extremities (hence the old name: Ray fungus).
- The disease spreads by direct invasion.
- In late cases blood stream spread may occur leading to lesions in the liver and brain.
- The organism cannot enter lymphatics, because of their large size; hence there is no lymphatic spread.

Clinical picture : Four clinical types are recognized :

Faciocervical type (60%) :

- This is the commonest type.
- A hard painless, non-tender mass appears in the parotid region, associated with trismus and thickening of the lower jaw.
- Multiple nodules then appear with softening and formation of abscesses and sinuses discharging pus and sulphur granules.
- The disease spreads with the formation of multiple sinuses and scaring of the neck.

2. Abdominal type (20%) :

- An indurated mass affects the appendix or ileocecal region and later invades the abdominal wall resulting in multiple sinuses.
- Occasionally the liver is affected by blood spread from the ileocecal region or from downward spread from the chest.
- The liver becomes enlarged and multiple abscesses are formed.

3. Thoracic type (15%) :

- The disease occurs by aspiration from the upper air passages or by direct spread from the neck or abdomen.
- Thoracic actinomycosis may give rise to cough, pleural pain, fever and weight loss simulating mycobacterial or mycotic infections.
- Later in the course of the disease the sinuses perforate the pleural cavity and the chest wall, often involving the ribs or vertebrae.

4. Cutaneous type (5%) : Rarely affected by direct inoculation.

Treatment :

- All forms of actinomycosis are treated with penicillin (5-20 million units daily) for many weeks.
- In addition, surgical excision or drainage of lesions or repair of defects may be required for cure.

Antibiotics in surgical infections

Choice of the suitable antibiotic :

Two factors should be considered; the patient & the known or likely causative organism. Factors including history of allergy to antibiotics, renal & hepatic function, resistance of the host, ability to tolerate oral drugs, race, age & if female, whether pregnant, lactating or taking an oral contraceptive.

The following guidelines are helpful whenever prescribing an antibiotic :

1. An initial diagnosis is essential before starting antibiotic therapy. Relevant samples should be obtained for culture and sensitivity testing before the first dose of antibiotic is given.
2. Length of course should be judged based on pathology, clinical and laboratory assessment.
3. The change from one antibiotic to another should be based on culture and sensitivity tests in association with clinical response.

Antibiotics in common use

[A] B-Lactam antibiotics :

Antibiotics in this group exert their activity on both Gram-positive and Gram-negative bacteria. They lead to inhibition of cell wall synthesis, and hence, cell lysis.

Four classes of antibiotics belong to this group :

1. Penicillins :

- Penicillin G : is effective mainly against Gram +ve bacteria such as streptococci and spirochaetes.
- Semisynthetic penicillins (e.g. methicillin) exert a wider activity against streptococcus and staphylococcus species.
- Ampicillin : lacks activity against some staphylococci but is active against enterococci and some Gram-negative bacteria.
- Combining amoxycillin with a lactamase inhibitor : (e.g. clavulanate) serves to extend the spectrum of activity against Gram-positive, Gram-negative aerobic & some anaerobic organisms.

2. Cephalosporins : Three generations have been described (first, second and third) :

- First : e.g. cephalothin, exert excellent activity against Gram +ve bacteria. Staphylococcal strains that are resistant to methicillin are invariably resistant to first generation cephalopsorins.
- Second : e.g. cefamandole have a slightly narrower Gram-positive bacterial spectrum but a much better Gram-negative aerobic activity.
- Third : is excellent anti-Gram -ve aerobic agents but their Gm +ve activity is variable. Selected agents e.g. moxalactam have excellent anaerobic activity while others e.g. ceftazidime are active against pseudomonas aereginosa.

3. Monobactams : are active only against Gram -ve aerobic bacteria. (Aztreonam)

4. Carbapenems : These agents have wide spectrum that includes Gram-positive bacteria, most Gram negative aerobes including pseudomonas, and anaerobes. Imipenem is the only currently available

[B] Aminoglycosides :

Effective mainly against Gram -ve aerobic organisms with little activity against Gram +ve or anaerobic bacteria. They act by interfering with bacterial protein synthesis. Commonly used agents belong to this group include gentamycin and amikacin. They all have considerable ototoxicity and nephrotoxicity.

[C] Quinolones : Quinolones exert activity against Gram-negative aerobic bacteria. Available agents include nalidixic acid, norfloxacin and ciprofloxacin. They are most commonly used in urinary tract infections.

[D] Glycopeptides : Agents belonging to this group (e.g. Vancomycin) possess activity against Gram-positive bacteria and are more potent than most other agents. They interfere with bacterial cell wall synthesis. They are effective against methicillin resistant Staph. as well as anaerobic Gram-positive cocci.

[E] Tetracyclines & chloramphenicol : Anaerobic Activity.

[F] Trimethoprim-sulphamethoxazole (Septrin) : effective against Gm -ve aerobic bacteria & some infections observed in immunosuppressed patients as with Pneumocystis carinii & Nocardia asteroids.

[G] Metronidazole : has excellent anaerobic activity but has no effect against aerobic organisms.

[H] Erythromycin : is a macrolide drug that exerts activity against Gram-positive bacteria and is usually used in patients allergic to B-lactam agents.

[I] Clindamycin : exhibits good activity against anaerobes and has some Gram-positive activity as well.

Complications of Antibiotics :

1. Hypersensitivity reactions.
2. Vitamin B deficiency with prolonged use.
3. Superinfections are caused by resistant strains.
4. Specific toxicities.

Burns

- Burns is one of the most serious injuries to the body.
- They cause dramatic damage to the physiological functions of the skin, which lead to serious local or systemic complications.
- By size and weight, the skin is the second largest organ in the body next only to the muscles
- Loss of large amounts of skin. if not replaced, is incompatible with life.

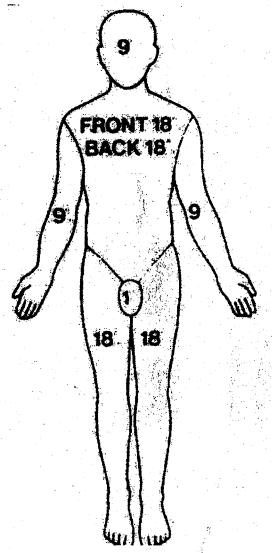
Etiology :

1	**Scalds**	Caused by boiled liquids.
2	**Flame burns**	Often due to ignition of clothing.
3	**Electric burns**	Blood & bones are good conductors, thus every organ in the body may be affected.
4	**Chemical burns**	Are due to either acids or alkalis.
5	**Inhalation burns**	Due to exposure to hot gases and may affect the upper or lower airway.

Classification :

[A] Classification according to the percentage surface area involved :

- This follows the rule of 9.
- In children he rule of 9 needs some modification due to the large size of the head in comparison to the rest of the body.
- **Burns are classified into :**



1	**Major burn**	Involves more than 30% of the body surface area.
2	**Intermediate burn**	Involves 15-30% in adults & between 10-30% in children.
3	**Minor burn**	Less than 15% in adults & 10% in children.

[B] Classification according to the depth of the burnt tissues :

1. First degree burns : The usual example is sunburns.
Only the epidermis is damaged causing erythema of the skin. They heal rapidly.

2. Second degree burns : The epidermis & a portion of the dermis are damaged.

- If no infection occurs, epithelial regeneration can occur from the remnants of hair follicles and sweat glands in the dermis and the burn will heal in 3 weeks.
- If infection occurs, these epithelial elements are destroyed and the case will be changed to a full thickness burn.

- This degree is further subdivided into :

(a) Superficial partial thickness burns :
Only the epidermis is damaged causing erythema of the skin. They heal rapidly.
(b) Deep partial thickness burns :
The epidermis and a portion of the dermis are damaged.

3. Full thickness burn : There is complete destruction of the epidermis and dermis.
After separation of the eschar by the third week, the patient should be prepared for skin grafting.

- The differentiation of partial thickness from full thickness bum is sometimes difficult and even in the same area.

- Both patterns may intermingle together. However, the following may help to differentiate :

Partial thickness burns	Full thickness burns
1. Mottled red.	1. White or black eschar.
2. Moist due to exudation of plasma.	2. Dry.
3. Shows blisters surrounded by erythema.	3. Possible visible thrombosed subcutaneous vessels.
4. Very painful and sensitive to air (pin-prick test).	4. Painless due to loss of the terminal nerve endings.
5. Should heal within 3 weeks.	5. Granulation tissue formation and eschar separation starts to occur after 3 weeks.

Epilation test : Useful test is to pull on a hair. If the hair pulls easily & painlessly, the burn is a deep one.

Histopathology :

- Temperatures greater than 45°C results in protein denaturation, which exceeds the capacity of cellular repair.
- Thermal injury to the skin results in 3 distinct zones :

1	**The central inner zone (zone of coagulation)**	If left, the eschar separates within 3 weeks leaving either a bed of granulation tissue (in full thickness burns) or a re-epithelialized bed (in partial thickness burns).
2	**The intermediate zone (zone of stasis)**	May die over the next 48 hours post-burn, if tissue oxygenation not maintained.
3	**The outer zone (zone of hyperemia)**	Tissues in this zone normally recover within 7-10 days unless subjected to infection.

- The rate of healing of burns depends on the surviving hair follicles and sweat glands.

Pathophysiology :

1. Increased capillary permeability leads to the loss of enormous amounts of fluids & proteins in the damaged area. It is maximum in the first 8 hours and continues for 48 hours.
2. Excessive loss of water by evaporation with loss of calories.
3. The burnt area will be colonized by bacteria.

Complications of burns :

I- Systemic complications :

1. Inhalation injury :

- Asphyxia may occur immediately from inhalation of heat or gases.
- Atelectasis, pneumonia, emphysema and pulmonary edema may follow.
- Finally respiratory failure may occur with systemic sepsis.

2. Neurogenic shock : is caused by pain.
3. Hypovolemic shock : may develop if the fluid losses are not properly corrected.
4. Renal failure : Acute renal failure can occur after prolonged uncorrected hypovolemia.
5. Gastro-intestinal complications :
(a) Acute ulceration of stomach and duodenum (Curling's ulcer) are rarely seen nowadays with the routine prophylactic use of antacids.
(b) Ileus usually occurs during the early post-burn period.
(c) Acute ulcerations of the colon.
(d) Multiple organ failure often follows sepsis. The outcome is poor.

II- Local complications :

[A] Early local complications :

1. Infection : Is the primary cause of death in burnt patients. Infection may lead to the development of septicemia and septic shock. It occurs usually between 4-7 days post burn. Treatment is essentially by prevention through proper local burn wound care and systemic antibiotic therapy.
2. Constricting eschars : May form in deep circumferential bums of the limbs and chest and should be treated by urgent escharotomy (release).
3. Edema : In burns of the face and neck, edema may lead to suffocation and urgent tracheostomy may be needed.

[B] Delayed complications :

1. Contractures across joints : Splintage and immobilization in the best functioning position with physiotherapy is important to prevent contracted scars.
2. Scar formation (hypertorophic or keloid).
3. Malignant transformation (Marjolin' ulcer) : In long standing unstable scars.

Management of burns :

[A] First aid management :

1. A patent airway should be assured.
2. A strong analgesic as 50mg pethidine is administered I.V.
3. Tetanus prophylaxis.
4. Saline or tap water, at room temperature, can be poured over the burnt area for 15 minutes to decrease edema and relieve the pain.

[B] Minor burns : (Less than 15% in adults and 10% in children)

- Can be treated as outpatient & treatment consists of :

1. Dressing, using the proper local chemotherapeutic.
2. Analgesia and systemic antibiotic prophylaxis.

[C] All majors and most moderate burns (except very superficial ones) should be admitted to the burn unit. :

1. A wide bore I.V. cannula is inserted rapidly.
2. A Foley's urethral catheter is introduced to check the urine output.
3. Treatment essentially consists of :

I- Resuscitative fluid therapy :

The amount and rate of fluid replacement :

- Depends on the weight of the patient and the percentage of the total body surface area injured.
- It is essentially give for the first 48 hours and after that.

The amount : The amount infused during the first 24 hours is 2ml/percent surface area burn/kg body weight. Half the amount calculated is given over the first 8 hours and the other half over the next 16 hours. Also half the calculated is given over the second day.

The types : The types of fluids infused vary in each formula.

1. Evan's Formula :

- **1st day:** 1 ml/kg/% burn normal saline + 1ml/kg/% burn colloid (Dextran) + 2000 ml glucose (Provided the daily caloric needs).
- **2nd day :** ½ ml/kg/% burn normal saline solution + 0.5 ml/kg% burn colloid + 2000 ml glucose.

2. Parkland's formula :

- 4ml/kg%burn lactated Ringer's solution/day.
- ½ the amount is given in the first 8 hours, ¼ in the second 8 hours, and ¼ in the third 8 hours.

It is to be noted that :

- In all formulae, the maximum percentage of burn calculated is 50%; otherwise serious over infusion may occur.
- Administration of blood can be started after 48 hours guided by the hematocrit value.
- Oral intake is avoided during the first 48 hours to avoid gastro intestinal complications and is started gradually after that.

How to judge the adequacy of intravenous resuscitation ?

1. Regular check-up of vital signs.
2. The urine output should be 30-60 ml/hour.
3. C.V.P. in critical cases.

N.B.: Patients who have extensive burns are liable to have a serious catabolic status. Introduction of intravenous hyperalimentation has made it easy to correct this problem and to support the patient nutritionally during this critical period.

II- Local burn wound care : (After resuscitation)

- **Constricting eschars** (in the limbs and chest) have to be released immediately. **Urgent fasciotomy** in deeper burns may be limb saving.
- **The aim** of the local wound care is to avoid infection.
- After cleansing & conservative debridement, **topical antimicrobial agents** should be applied.
- **The wound is managed by either :**

1. The exposure method :

- Exposure method requires isolation of the patient in completely aseptic atmosphere.

Advantages :

1. It is more comfortable to the patient.
2. It avoids the need for repeated change of dressings, which implies a great burden on nursing staff and is rather expensive.
3. It inhibits the growth of bacteria by the dry air surrounding the burn.

Indicated for :

1. Burns of the face, neck and perineum.
2. Burns involving one side of the trunk.

2. Bulky occlusive dressing (the occlusive method) :

Dressing change is the occlusive method can be done by the use of a special tub (Hubbard Tank) or under anesthesia (especially in children) since h is usually very painful and adherent.

- **Both occlusive and exposure methods are equally effective.**
- **All partial thickness burns should heal within 2-3 weeks.**
- **Full thickness bums will require closure by autogenous skin grafts.**

[D] Later care :

Following the previous regimen of wound care, all partial thickness burns should heal within 2-3 weeks, while full thickness burns will require closure by autogenous skin grafts. For deep burns :

1. Autologous skin grafting :

- Partial thickness skin grafts (Thiersch grafts) are commonly used to cover the large raw areas produced by burns.
- A graft is applied after either spontaneous separation of eschar (3-4 weeks), or early burn wound excision.
- Early burn wound excision is the preferred method for deep burns of the hand.

- Patients are usually subjected to surgery 3-5 days post-burn (before bacterial infection sets in), where tangential excision of the damaged dermis is carried on. When healthy bleeding tissues are reached a skin graft is applied.

2. Biological dressings :

- **Indications :**

1. Autograft is not enough.
2. Local wound condition is not favorable.

- **Advantages :**

1. The wound will be less painful.
2. Minimize fluid and protein loss.
3. Control infection.

- **Examples :**

1. Allografts (Cadaver's skin).
2. Xenograft skin (Pig's skin).
3. Amniotic membrane.

- Applied after removal of the eschar and are changed every 3-4 days.
- It is only temporary and permanent closure can be achieved only by autograft skin.
- Artificial skin substitutes are used with promising results.

3. Prevention of contractures : Contraction is a normal component of wound healing and its prevention across joints can be achieved by proper splintage, immobilization in the best functioning position, and.physiotherapy.

Prognosis of burns

[A] Burn factors :

1. Extent : This is the most important factor. Mortality is about 50% if the extent of burn is 50%.
2. Depth : Deeper burns carry higher mortality and more disfigurement.
3. Site : Burns of the face are the worst because they are likely to be accompanied by inhalation burns of upper and lower respiratory tracts.
4. Infection : Septicaemia is the major killer of burn victims.
5. Type : High-voltage electric burns are the worst. They are usually fatal. Scalds with boiling water commonly cause superficial burns and are the least harmful.
6. Associated injuries.

[B] Patient factors :

1. Age : Burn victims at extremes of age (children and elderly) have bad prognosis.
2. Concomitant diseases e.g. diabetes and coronary heart disease.

[C] Treatment factors :

Patients who are treated in **specialized centres** have better chance of survival and avoidance of complications.

Special Types of Burns

[A] Electric burns : (A form of thermal injury)

- **Severity of the burn :** It is divided into high and low-tension injuries according to the voltage responsible for the injury (whether above or below 1000 volts).
- **Tissue damage is due to :** the passage of the electric current through blood and bones.
- **The affected blood vessels** usually show late thrombosis with delayed progressive ischemic necrosis at different sites.

[B] Chemical burns :

- **Tissue damage is due to :** Oxidation, reduction, corrosion or protoplasmic poisoning.
- **Severity of the burn :** is determined by the strength of the agent, its amount, duration of skin contact and its mechanism of action.
- **Management :**

1. Systemic control by administering the proper antidote in case the agent is absorbed.
2. Locally, the agent should be thoroughly cleansed; all saturated clothes are removed and affected areas irrigated with massive amounts of water.

Treatment of special burns

1. Burns of the face : The aim :

(a) Is to keep the skin movable.
(b) To care for the eyes and ears.
(c) Obtain good cosmetic result :

- Where the burn extends into the scalp, the hair is shaved for at least 2 inches beyond the burn. The burn is best treated by exposure but deep burns require early grafting either after initial excision or as soon as the eschar begins to separate.
- In burns of the eyelids, the splinting action of the crust may lead to exposure keratitis, which should be avoided by the frequent application of Vaseline or cold cream. If the eye is injured, the conjunctival sac should be irrigated with normal saline and cocaine hydrochloride is instilled to alleviate the pain.
- In burns of the ears, infection should be avoided to prevent exposure of the cartilage.

2. Burns of the hand :

- The usual treatment is by occlusive dressing with the application of a plaster slab to ensure immobilization and facilitate elevation.
- The dressing is left for 12 - 15 days by which time superficial burns are healed but deep burns will require grafting after a further l0 days of preparation.

3. Burns of joint surfaces :

- Exposure treatment with hydrotherapy and physiotherapy is the best method.
- In deep burns, early skin grafting is essential to obtain a good functional result and avoid contractures and deformities.

4. Burns of the perineum :

- The best treatment is by exposure and topical silver sulfadiazine applications.
- In burns of the penis, the external meatus should be attended to, in order to prevent stricture, and in burns of the vulva a pledget of gauze or cotton wool should be inserted between the labia to prevent adhesions.

Principles of skin coverage

Skin defects represent one of the common problems in surgical practice.

Etiology : Trauma, burns or following the surgical resection of different benign and malignant lesions.

I- Skin grafts : There are two Types of skin grafts :

	1. Split thickness (Thiersch) graft	2. Full thickness (Wolfe) graft
Includes	Epidermis & part of dermis.	Epidermis & the full thickness of dermis.
Advantages	1. Good take. 2. Donor site heals spontaneously.	1. Minimal contraction 2. Resistant to trauma. 3. Better sensation. 4. Aesthetically better.
Disadvantages	1. Maximum contraction. 2. Weak resistance to trauma. 3. Poor sensation. 4. Aesthetically poor.	1. Less take. 2. Donor site must be closed surgically. 3. Donor sites are limited.
Sites	Hidden areas e.g. thigh.	1. Above the clavicle. 2. Behind the auricle.

Composite graft : Is skin graft, which includes an underlying tissue e.g. subcutaneous tissue, muscle, cartilage or bone.

Graft survival :

- The vascular status of the bed determines the survival (take) of a skin graft.
- Bare conical bone (devoid of periosteum), bare tendon, and bare cartilage will not take a skin graft.

Take depends upon :

1. The status of the recipient bed.
2. The graft thickness **(the thinner the graft, the faster is the take).**
3. The size of the graft **(a small graft takes rapidly).**

II- Flaps :

Definition : Tissues transferred from one site of the body to another with their blood supply.

1. Skin flaps :

- These can be classified : 1. Local flaps. 2. Distant flaps.
- According to vascular pattern flaps are classified into :

(a) Random pattern flaps with no anatomically recognized blood supply. They have a strict length to width ratio of 2:1 & maximally not exceeding 3:1.

(b) Axial pattern flaps supplied by a known artery. They may retain their skin attachment to the donor area & are termed pedicled flaps, if not, they are termed island flaps.

2. Musculocutaneous (myocutaneous) flaps : these are axial flaps that receive their blood supply from the underlying muscles through perforator vessels. A famous example is the latissimus dorsi myocutaneous flap & the pectoralis major myocutaneous flap.

3. Fasciocutaneous flaps : they have the same principles as the previous one, but their blood supply is through fasciocutaneous perforators.

4. Microvascular free flaps.

III- Tissue expanders : Tissue expanders are inflatable silicon implants. They are placed subcutaneously in collapsed state. Over several weeks the expanders is gradually inflated with saline through a subcutaneous port. The overlaying skin is gradually stretched to accommodate a larger area. Finally, the expanded skin can be used to cover defects & the tissue expander is removed.

Aesthetic surgery

Definition : This is surgery intended to improve the appearance.

Examples : 1. Rhinoplasty. 2. Face lifting. 3. Eyelids surgery. 4. Liposuction.
5. Breast surgery e.g. augmentation mammoplasty and reduction mammoplasty.

Surgical nutrition

Entral nutrition

Indications :

Indicated in patients in whom oral intake is inadequate or impossible, while having a functional accessible gastrointestinal tract as in unconscious patients, severe dysphagia & head & neck surgery.

Route of administration :

Through a nasogastric tube, or through a surgical or percutaneous intubation of the upper gastrointestinal tract e.g. gastrostomy or a jejunostomy.

Administration regimens and formulae :

For stomach, liquid diets formed of soups, juice, milk, and blenderized food is generally well tolerated if administered at a reasonable rate. The jejunum, on the other hand, is highly sensitive, and feeding should be started with isotonic, sterile formulae at a slow rate.

Complications :

1. Mechanical complications : Pharyngeal and oesophageal mucosal irritation and ulceration, obstruction of the feeding tube lumen, and tube displacement.
2. Gastrointestinal complications : Nausea, vomiting and pulmonary aspiration, distention.
3. Metabolic complications : e.g. glucose intolerance & electrolyte imbalance.

Parental nutrition

Indications :

1. For the malnourished or the hypercatabolic patient with failure of nutrients absorbtion e.g. massive bowel resection, severe inflammatory bowel disease.
2. Preoperative to the severely debiliataed patient 10-14 days prior to operation reduces postoperative mortality.

Route of administration :

Central venous catheter inserted percutaneously through either the subclavian, or the internal jugular vein, and threaded forward so that its tip will lie in the superior vena cava.

Administration regimens and formulae :

The daily requirements are estimated according to the body weight & to which are added the deficits :

- Carbohydrates are provided by 20% or 50% glucose.
- Proteins are administeted as L-amino acids solutions that should contain the essential members.
- Fat emulsions are produced from soya oil (Intralipid) & are available in 10% & 20% concentrations

N.B: Home parenteral nutrition:

Intravenous nutrition at home is usually reserved for patients who had massive small intestinal resection (short bowel).

Monitoring :

1. Measuring the body weight is done daily.
2. Daily balance of fluid intake and output.
3. Estimation of plasma proteins, serum calcium, magnesium and phosphate, liver function tests, and blood coagulation studies.
4. Manifestations of sepsis are always searched for.

Complications :

[A] Nutritional and metabolic complications : e.g. hyponatremia, hypokalemia, or hyperglycemia.
[B] Catheter Complications :

1. Misplacement of the catheter.
2. Insertion of the catheter tip into the pleural cavity, hemothorax or pneumothorax.
3. Air can be sucked into the superior vena cava.
4. Venous thrombosis.
5. A common serious complication is the central venous catheter infection, and septic thrombophlebitis which lead to septicemia and, if neglected, death.

Malnutrition in surgical patients

Causes :

The two principal causes of malnutrition in surgical wards are starvation and the catabolism of surgery and trauma and their complications.

Starvation :

1. Social causes as poverty, and the neglected elderly.
2. Dysphagia e.g. carcinoma of the esophagus.
3. Loss of appetite by visceral malignancy e.g. carcinoma of the stomach.
4. Repeated vomiting e.g. pyloric stenosis.
5. Malabsorption e.g. extensive inflammatory bowel disease.
6. Extended postoperative restriction of oral intake.

Hypercatabolism :

1. Major trauma and burns.
2. Major surgical procedures.
3. Severe acute pancreatitis & major sepsis e.g. peritonitis and septicemia.

Effects of malnutrition on the outcome of surgery :

1. Impairment of wound healing.
2. Suppression of immune response and a higher susceptibility to infection.
3. A sense of mental and physical exhaustion that delays recovery.
4. Reduced tolerance to radiotherapy and anticancer chemotherapy.

Diagnosis :

There is a very wide range of tests, some of which are highly sophisticated, for the assessment of the degree of nutritional impairment. Some of the simpler indications of malnutrition are mentioned below.

Anthropometric measurements:

1) Recent unintentional weight loss of 10% or more.
2) ***Body weight*** is less than 80% of ideal for height. Body mass index ***(BMI)*** =weight kg/ (height in metres)^2.
3) Mid-arm muscle circumference is less than 80% of value in comparable population. It correlates with the skeletal muscle mass.
4) Triceps skin fold thickness, measured by the use of a caliper, is an indication of fat loss. The average thickness in females equals 13 mm and in males 11 mm.

Laboratory tests :

1. Serum albumin.
2. Daily nitrogen balance.

Immune functions : Total lymphocyte count below 1.2 x10^9/L.

N.B:Morbid obesity is defined as being 100 pounds above ideal weight, twice ideal body weight, or having a BMI (measured as weight in kilograms divided by height in meters squared) of 40 kg/m^2. The latter definition is more accepted internationally, and has essentially replaced the former ones for all practical and scientific purpose.

Transplantation

Organ donation

Donor types :

[1] Living donor : paired organs e.g. kidney & vascularized segmental pancreatic & liver transplantation.

[2] Cadaver donors : this method avoids the risk of complications, which may occur to the living donors and has the advantage that multiple organs can be taken from one cadaver and transplanted to many patients with brain stem death. The criteria of brain stem death are :

1. Deep coma (no response to external stimuli).
2. Bilateral dilated fixed pupils.
3. Absence of all reflexes (gag, corneal, etc).
4. Inability to maintain the vital signs for three minutes without artificial means.
5. Flat EEG in all channels (i.e. absence cortical activity).

Organ Preservation :

1. Cooling (surface or perfusion) down to 0-4°C to reduce tissues metabolism.
2. Perfusion of a special fluid medium to prevent cellular edema & maintain vitality.

Renal Transplantation	Hepatic Transplantation	Pancreatic Transplantation
Indications		
All cases of end-stage renal disease which may be secondary to : 1. Glomerulonephritis (most common cause). 2. Hypertension. 3. Diabetes. 4. Chronic Pyelonephritis. 5. Polycystic disease. 6. Lupus nephritis. 7. Obstructive uropathy. 8. Congenital nephrotic syndrome. • If a related living donor is available and willing, then early transplantation is indicated even before the start of hemodialysis. • If the living related donor is not available, the patient is immediately placed on a cadaver donor list (not legalized in Egypt).	**1. In children :** • Cirrhosis due to biliary atresia, congenital hepatic fibrosis, and congenital hepatic cirrhosis. • Metabolic disorders as glycogen storage disease, alpha 1 antitrypsin deficiency, galactosemia and histocytosis. **2. In adults :** • Cirrhosis : Primary & secondary biliary cirrhosis, chronic active hepatitis, sclerosing cholangitis and alcoholic cirrhosis (relative indication). • Metabolic : Hemochromatosis, Wilson's disease and Budd-Chiari syndrome. • Neoplastic : The tumor should be localized and there should be no evidence of metastases.	1. Type 1 insulin dependent diabetes mellitus with renal failure. Combined renal and pancreatic transplantation is performed. 2. Patients with previous renal transplantation suffering from severe diabetes.
Technical consideration		
1. The grafted kidney is placed in an extraperitoneal position in the iliac fossa (preferably the right one). 2. The arterial anastomosis is performed between the renal artery and the external iliac or internal iliac artery. 3. The venous anastomosis is performed between the renal vein and the external iliac vein. 4. The ureter of the grafted kidney is anastomosed to the patient's urinary bladder.	**Orthotopic Liver Transplantation:** The liver of the recipient is removed. The new cadaveric liver graft is placed in the same position of the original liver and the following anastomoses are performed in order : 1. Suprahepatic IVC. 2. Infrahepatic IVC. 3. Portal vein of recipient to donor. 4. Hepatic artery of recipient to donor. 5. Common bile duct of recipient to donor. Nowadays, segmental liver transplantation from living donors are being successfully performed.	**There are two types of pancreatic transplantation :** 1. Vascularized pancreatic transplantation : Whole or segmental pancreatic transplantation is performed. 2. Islets of Langerhans implantation (still under study).
Complications		
1. Technical complications include arterial and venous occlusion or stenosis, bleeding and leakage. **2. Rejection.** **3. Recurrence** of the original disease in the grafted organ. **4. Complications of immunosuppression.**		
Results		
1. Cadaveric donor: 1-year graft survival is 95%. **2. Living related donor:** 1-year graft survival is 98%.	1-year graft survival is 85%.	1-year graft survival is 45%.

Principles of immunosuppressive therapy

According to their mode of action, drugs used in clinical immunosuppression are classified into 2 groups :

[A] Drugs which deplete circulating lymphocytes :

1. Corticosteroids

2. Anti-lymphocytic globulin (ALG) and antithymocytic globulin (ATG) :

3. Monoclonal antibodies (OKT_3)

[B] Drugs which inhibit lymphocyte activation or proliferation :

1. Cyclosporine : It suppresses T-cells& blocks release of IL-2.
Side effects : Include nephrotoxicity, hepatotoxicity, neurotoxicity, hypertension and hyperkalemia.

2. Tacrolimus (FK_{506}) : It arrests T-cell activation and it is 100 times more potent than cyclosporine.
Side effects : Are similar to cyclosporine.

3. Azathioprine : It is metabolized to 6-mercaptopurine that inhibits the division and differentiation of immunocompetent lymphocytes.
Side effects : Hepatotoxicity and leucopenia.

In addition to the previous specific side effects all immunosuppressive drugs have two more side effects :

1. Infections : Various viral, bacterial or fungal infections may arise in the respiratory or urinary tracts, intra-abdominally or at cannulation sites.

2. Neoplasia : Prolonged immunosuppression predisposes to the development of skin cancer, lymphomas and cervical carcinoma

Methods of immunosuppression

[A] Induction immunosuppression :
The first two weeks after transplantation are very important in preventing the lymphocytes from attacking the transplanted organ. This is achieved by :
1. Large doses of corticosteroids. 2. Azathioprine. 3. Antithymocyte globulin (ATG).

[B] Maintenance immunosuppression :
1. Cyclosporine. 2. Small doses of corticosteroids. 3. Azathioprine.

[C] Anti-rejection treatment :
1. Selective destruction of subsets of T-lymphocytes responsible for graft destruction (OKT_3 is a monoclonal antibody against T-lymphocytes carrying CD3 receptors).
2. High doses corticosteroids.

N.B: Organ transplantation definitions:

- **Autografts**: same individual is donor and recipient.
- **Isografts**: tissue transfer from an identical twin, no rejection.
- **Allograft**: donor and recipient are genetically dissimilar but of the same species.
- **Xenograft**: donor and recipient belong to different species (animal to man).not practical.

How cancer arises ?

Gene mutations :
Malignant transformation of a cell occurs through accumulation of mutations in specific classes of genes within it. Two gene classes, together constitute only a small proportion of the full genetic set, play major roles in triggering cancer, in their normal structure, they ensure normal controlled cell growth & division.

1. Proto-oncogenes : encourage such growth. When mutated, proto-oncogenes can become carcinogenic oncogenes

2. Tumor suppressor genes : normally inhibit abnormal eel! growth and division. They contribute to cancer when they are inactivated by mutations. Examples are :

- P53 suppressor gene is involved in a wide range of cancers.
- BRCA1 suppressor gene is involved in breast and ovarian cancers.
- BRCA2 suppressor gene is involved in breast cancer.

Escaping the body defense mechanisms :

The human body contains about 30 trillion cells; thousands of them become mutated and cancerous everyday. Our bodies are equipped with checking systems that continuously eliminate them, and only rarely does a cancer cell continue to live and to replicate producing a frank malignancy.

1. Apoptosis (Programmed cell death).
2. Immune system.

Etiology of cancer :

Cancer seems to arise from the effects of two different kinds of carcinogens.

1. Agents that damage genes involved in controlling cell proliferation and migration. These initiate the malignant transformation (oncogenesis) :

(a) Chemical & physical carcinogens.
(b) Viruses & diet.
(c) Idiopathic.

2. Agents that selectively enhance the growth of tumor cells or their precursors, e.g., hormones :

(a) TSH stimulates growth of papillary carcinoma of the thyroid.
(b) Estrogens & Progesterone stimulates growth of breast cancer.
(c) Androgens stimulate growth of prostate cancer.

Chemical carcinogens : Tobacco smoke & occupational carcinogens.

Physical carcinogens :

- Continuous mechanical irritation
- Ionizing radiation & Ultraviolet (UV) radiation.

Viruses :

Both RNA and DNA viruses but the commoner cancer-causing pathogens are the DNA viruses.

- Human papilloma viruses can lead to cancer of the cervix, and anus.
- Hepatitis B and C viruses can cause hepatocellular carcinoma.
- EBV can cause nasopharyngeal carcinoma & Burkitt's lymphoma.

Diet :

- Animal (saturated) fat&red meat are strongly linked to malignancies of the colon and rectum.
- Consumption of alcoholic beverages increases risk of cancer of the upper digestive tract.

Idiopathic .

Stages of cancer development :

1. Hyperplasia. 2. Metaplasia.
3. Dysplasia. 4. In situ cancer.
5. Invasion. 6. Metastasis.

Cancer grading :

Grading is a measure of tumor aggression. This largely depends upon its differentiation.

- Well-differentiated tumors.
- Moderately-differentiated tumors.
- Poorly-differentiated and undifferentiated tumors.

Spread of cancer :

- **Properties that allow metastasis :**

1. Defective cell adhesion.
2. Tumor angiogenesis.
3. Production of proteolytic enzymes that digest the basement membrane,capillary&lymphatic walls.
4. They escape apoptosis.

- **Modes of metastasis**

1. Local spread 2. Lymphatic spread.
3. Blood-born spread. 4. Trans-celomic spread.

Diagnosis :

[A] Early detection of asymptomatic cases (screening) e.g. :

1. Annual soft tissue mammography for females at risk of breast carcinoma.
2. Annual colonoscopy for patients with ulcerative colitis at risk of colo-rectal cancer.
3. Annual prostate specific antigen (PSA) for men above fifty.

[B] Diagnosis of symptomatic cases :

The aim is to diagnose the disease and to determine its extent (stage).

1. Thorough clinical assessment.
2. Radiology & endoscopy.
3. Tumor sampling by Tissue biopsy & Cytology.
4. Tumor markers :

- **Many malignant tumors secrete certain oncofetal proteins e.g. :**

(a) α-feto protein : Hepatocellular carcinoma & non-seminomatous testicular tumors.
(b) Carcinoembryonic antigen : In carcinoma of gastrointestinal tract, pancreas and breast.
(c) Prostate specific antigen : Is raised in prostatic carcinoma.
(d) CA 15-3 : Is raised in carcinoma of the breast.
(e) CA-125 : Is raised in carcinoma of the ovaries.
(f) CA 19-9: Is raised in carcinoma of the gastrointestinal tract and pancreas.
(g) Thyroglobulin : Is raised in carcinoma of thyroid.

- **Tumors from endocrine glands, especially if benign, secrete hormones of the glands from which they arise. Examples include :**

(a) Pituitary tumors : Secrete trophic hormones as ACTH.
(b) Pancreatic islet tumors : Secrete insulin, glucagon or somatostatin.
(c) Parathyroid tumors : Secrete parathormone.

Treatment :

[A] Prophylactic treatment :

Certain precancerous lesions are well known and their eradication can prevent the development of cancer. A well known example is familial polyposis of the colon which is one hundred per cent premalignant. Total proctocolectomy protects the patient from the subsequent development of large bowel cancer.

[B] Treatment of established cases :

1. Early (equivalent terms = loco-regional, potentially curable, operable) cancer :

- There is no evidence of distant spread & Cure is possible if this local disease is eradicated.
- Treatment is radical i.e., aims at cure & is by loco-regional modalities i.e. surgery, radiotherapy or a combination of both.
- Adjuvant treatment of systemic modalities such as chemotherapy is indicated if there is a high possibility of systemic microscopic spread in distant sites.

2. Late (equivalent terms = systemic, incurable, inoperable) cancer :

- There are distant metastases & Cure is not possible.
- Treatment aims at palliation of the patient's symptoms & is done by systemic modalities as chemotherapy and hormonal treatment.
- Surgery or radiotherapy is sometimes needed to palliate local symptoms.
- Pain relief is accomplished by the administration of non-steroidal anti-inflammatory agents or narcotic analgesics. In severe cases neurosurgical procedures to interrupt pain pathway

[C] Individual modality treatment includes :

1. Surgery:

- **Primary tumor :** Radical surgery
- **Lymph nodes :** Block excision.
- **Precautions :** During surgery care is taken to avoid spillage of malignant cells.
- **Advantages :** Surgical excision is both quick & effective. & is also the one method of therapy that offers the opportunity to confirm that a tumor has been fully excised.
- **Disadvantages and limitations :** Surgery may produce functional and cosmetic disabilities & can't be applied if the tumor is fixed to a vital structure or if it has produced distant spread.

2. Radiotherapy :

- **May replace surgery** or may be given in addition.
- **Method :** Powerful X-rays, gamma rays, electrons, or heavy particles.
- **Advantages :**

1. It can preserve the anatomical structures that surround a cancer growth.
2. It can destroy microscopic extensions of cancerous tissue around a tumor.
3. It is a safer option for older, frailer patients.
4. Patients treated with radiation usually do not require hospitalization,

- **Disadvantages :**

1. Some tumors are not sensitive to irradiation.
2. It is commonly associated with bums of the skin or enteritis.
3. Compared to surgery, radiotherapy is slower

3. Chemotherapy :

- **Common indications :** Leukemias, solid tumors.
- **Combination chemotherapy :** Is better than single agent chemotherapy.
- **Prevent cells from multiplying** by interfering with their ability to replicate DNA.
- **Advantages :** Systemic action.
- **Disadvantages :** Tendency to damage to the rapidly growing cells e.g. cells of the bone marrow causing anemia, leucopenia and thrombocytopenia. Other side effects of chemotherapy include diarrhea, nausea vomiting and hair loss.

4. Hormone therapy :

Hormone-blocking and hormone-supplementing therapies affect the rate at which tumor cells grow and multiply. It is of fewer side effects. E.g. :

- Anti-estrogens for women with breast cancer that is positive for estrogen receptors.
- Androgen blockade for men with prostate cancer.
- Thyroxin to suppress TSH for patients with papillary carcinoma of thyroid.

5. Immunotherapy :

- **Non-specific :** The BCG vaccine to increase immunity& found to induce remission in cases of transitional cell carcinoma of urinary bladder.
- **Specific :** Monoclonal antibodies.

6. Bone marrow transplantation : Is sometimes used to strengthen the depleted bone marrow.

7. Biological therapy:

New advances in molecular biology allowed production of newer anti-cancer drugs which antagonize certain biological agents produced by certain tumors.**e.g**
Herceptin: against Her-2 neu receptors in breast carcinoma.

Prognosis :

Factors affecting prognosis :
1. Tumor : Stage (most important factor), Grade of malignancy and differentiation, Site & Type.
2. Management : Early detection & proper treatment.
3. Patient : Age of patient, Presence of concurrent debilitating illness & Immuno-suppression.